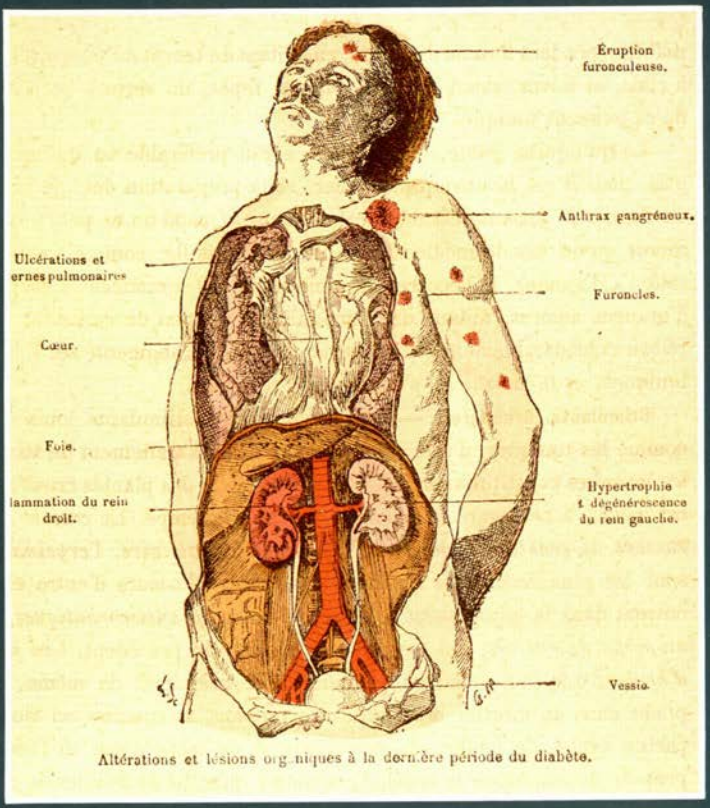
DIABETES

A model for health care management



Altérations et lésions organiques à la dernière période du diabète.

DIABETES

A model for health care management

This paper was researched and written by William Laing and Rhys Williams.

Foreword by Lord Butterfield.

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Office of Health Economics

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Foreword

Since the Office of Health Economics first published a paper about diabetes 25 years ago a great deal has happened.

For one thing diabetes mellitus has been accepted as an international problem by the World Health Organisation. Professor Hoet, father of the present Professor of Medicine at Brussels University and currently the President of the International Diabetes Federation, played a major role in achieving this in the 1960s. Until then the Geneva Head Office had put the condition aside as a disease of affluence, of no particular concern to an Agency like WHO primarily concerned with helping developing nations. I know it seemed then to some WHO staff a dubious investment of their resources, but as things have turned out, the decision is now paying handsome health dividends.

By taking the initiative of the 1960s, WHO proposed levels of blood glucose for the diagnosis of diabetes and how to measure them. This was an essential step forward. It tidied up an unsatisfactory ethical state of affairs: countries with predominently private practice medicine were interested in setting low criteria to raise the number of cases for the physicians' offices appointment books. By contrast, health administrators generally wanted a diagnostic level above which expensive complications would usually be an added burden on health services. International administrators and those interested in the anthropology of diabetes needed agreed diagnostic levels to ensure comparability of the many epidemiological studies emerging everywhere. As it has turned out, all this has given insight into the ways diabetes affects unsophisticated populations when they are exposed to modern life-styles. As the New Zealander, Ian Prior said, in the Pacific Isles an outboard motorboat engine may precipitate diabetes in a Polynesian fisherman used to paddling and sailing his boat.

So the excellent paper published here by William Laing and Rhys Williams, looks at diabetes worldwide, not just in Britain as its predecessor did. The section on epidemiology in different countries is bound to interest readers in all parts of the world. So will the authors' careful studies of the prevelances of various diabetic complications, in various circumstances and in various countries. In older patients these complications are often the first symptoms of the disease, bringing the patient to the doctor.

Interest in the molecular biology of diabetic complications, including the accumulation of sorbitol in some cells in diabetics, has also grown in the last quarter of a century. Since Max Perutz patiently unravelled the complex structure of haemoglobin molecules, it has become apparent that during their exposure in red cells to ambient glucose levels for over one hundred days, certain constituent amino-acids take up glucose and the haemoglobin becomes glycosylated. This changes the physical characteristics – the electrophoretic migration, which makes it possible to determine the percentage prevalence – up to 8.5 per cent or so in normal people. Exposure to high glucose concentrations results not only in a rise in this percentage, but there have also been reports of a reduc-

tion in the efficiency of the glycosylated haemoglobin molecule unfolding to accept and deliver oxygen molecules to the tissues.

Similar glycosylation almost certainly occurs in other structurally important proteins with a slow body turnover and may change their biophysical functions too. Glycosylation may lie behind lens changes in the eye and probably in the changes in the capillary basement membranes. Naturally, over the last quarter of a century, these ideas have reinforced the epidemiological and community studies which laid increasing emphasis on the need to control diabetics' glucose levels. This puts extra work on physicians and their support workers. If they are going to control the complications and avoid serious impact on patients health through diseases in the heart, stroke, the peripheral vessels, the kidneys, the retinal capillaries as well as the optic lenses, the peripheral nerves, the skin and so on, diabetologists need to know personal glucose levels at home. This has become possible with new, though expensive, devices. So the way ahead seems clear if demanding.

The overall burden of diabetes on health care services has been increased, and further aggravated by rising prevelences of obesity and therefore of non-insulin dependent diabetics – as well as by longer lives, especially in the emerging nations. All this means that WHO's very proper primary concern with preventive medicine can move from the successes of vaccination to the long drawn out, intractable problems of the control of diabetes. Painstaking medical care, based on careful personal education of each diabetic case and proper therapy, can and will make major medical and economic contributions to human wellbeing worldwide.

John Butterfield

Introduction

At the beginning of the century, before the advent of insulin, most young people diagnosed as having diabetes died within two years of onset. After the introduction of insulin, mortality rapidly dropped. Records from the Joslin Clinic in Boston, Massachusetts show just how dramatic the change was.

Treatment of insulin dependent diabetes is thus one of the great success stories of modern medicine. Furthermore, because the dose of insulin has to be adjusted to the individual patient, and varied according to their diet and amount of exercise, insulin heralded many of the ideas involved in modern therapy needing careful surveillance and adjustment. But success has brought new problems. People who would previously have died now live, though frequently with impaired health, to consume a substantially higher than average amount of healthcare resources. It is estimated that between one and five per cent of the population in developed countries suffer from diabetes and often account for a larger proportion of health care costs. In Britain, for example, people diagnosed with all forms of diabetes make up something over 1 per cent of the population[1] but absorb about 4-5 per cent of health spending. In the United States, an estimated 2.7 per cent of the population has diabetes but absorbs about 5 per cent of health spending.

In the Third World, however, the problems posed by diabetes are of an entirely different magnitude. In some developing countries it is estimated that as many as 30-35 per cent of the adult population suffers from diabetes. This has led the World Bank to describe the health and economic problems facing these countries as a 'time bomb'. The effects of this extremely high prevalence of diabetes on the economic wellbeing of these countries is, as yet, unquantified but is likely to be considerable. The development of measures to reduce the burden of diabetes in these societies is of vital importance. The close relationship between diabetes and other diseases previously viewed as 'diseases of affluence' such as hypertension, ischaemic heart diseases, obesity and cerebrovascular disease means that it cannot be viewed in isolation from them. The emergence of these diseases in the Third World has reached a critical point when, unless their causes and effects are understood and unless effective preventive measures are introduced, they will replace communicable diseases, famine and high infant mortality as the most important influences on the health of the society.

In developed countries, diabetes remains a major but containable health problem. In Britain, the 1970s saw the centre of gravity of diabetes management shift away from hospitals and towards the community and this seems to have paid off in the 1980s with a reversal of the previously rising trend in hospitalisation for acute episodes of diabetes – in contrast to the United States, where no such reversal of trends has been observed.

It is increasingly recognised that, in the absence of primary preven-

1 There are probably as many again who have signs of the disease without being diagnosed.

Table 1 **Death rate per 1,000 diabetic patients* at specified ages, Joslin Clinic, Boston, Massachusetts, 1897–1961**

Age at Death (Years)	*Naunyn Era†*	*Allen Era†*	*Insulin Era*				
	1897–1914	*1914–1922*	*1922–1926*	*1926–1929*	*1929–1938*	*1939–1947*	*1950–1961*
10	824.0	386.1	61.4	19.1	8.1	3.3	1.0
20	614.0	410.8	89.4	18.3	12.6	7.9	3.4
30	359.8	236.8	74.8	33.4	13.9	11.3	14.4
40	165.7	115.1	34.7	23.8	16.6	13.6	15.3

*Excludes deaths within 1 week of first observation or hospital discharge.
†Naunyn and Allen were physicians specialising in the treatment of diabetes.

Source Marks, H H. Longevity and mortality of diabetics. *Am J Public health* 55:416–23, 1965.

tion, the key to further reducing the burden of diabetes lies in the development and refinement of more effective systems for the long-term management of the disease and its complications. There has been a good deal of innovation and experimentation with the content and location of services for people with diabetes. For Britain, a major question now is whether the reforms proposed in the government's 1989 White Paper on the National Health Service *Working For Patients* will encourage or inhibit continued experimentation involving trade offs between hospital and primary care. There is also the question of how to encourage the detection of late-onset diabetes where the classical symptoms are often absent.

What is diabetes?

History

Diabetes has been recognised from ancient times as a disease characterised by weakness, thirst and frequency of micturition[2]. Aretaeus, a contemporary of Galen, noted that the Greek word for a siphon (διαβητησ) had been given to diabetes because 'the fluid does not remain in the body, but uses the body as a ladder, whereby to leave it.' In modern times, the sweet taste of urine passed by people with this disease was noted by Willis in the late seventeenth century and Matthew Dobson of Liverpool demonstrated that the sweet taste was due to sugar by fermenting the residue remaining after evaporation. In 1815 the French chemist Chevreul showed that the sugar in diabetic urine is glucose. The association between diabetes and the pancreas was not recognised until much later. In the mid 19th century Langerhans described the islets of tissue scattered throughout the pancreas, which were later given his name, but it was not until 1889 that von Mering and Minkowski produced rapidly fatal diabetes by excising the pancreas in animals and went on to demonstrate that the disease was not due to interruption of the flow of pancreatic juice to the bowel, but that the pancreas exerted its influence on metabolism by a systemic effect.

The discovery of insulin, the active principle of the islets of Langerhans was made in 1921 by Banting and Best in Toronto. Insulin was isolated by Abel in 1926. Though injection with insulin from animal sources revolutionised treatment, the first hopes that diabetes was no more than a deficiency disease, requiring simple replacement therapy, soon proved to be unfounded. During the thirties and forties research revealed more complex physiological functions which can play a part in the aetiology of the disease and in the development of diabetic complications. It was also recognised that there were a number of different forms of diabetes, not all requiring insulin therapy, and these have since been separated into two main entities, insulin dependent diabetes mellitus (IDDM) and noninsulin-dependent diabetes mellitus (NIDDM). More

2 These classical symptoms of diabetes are much less commonly present in patients developing the disease later in life, and this makes the detection of late-onset diabetes more difficult.

recently attention has turned to cell surface receptors responsible for receiving chemical messages from insulin and other hormones and the search for the causes of diabetes has turned away from purely endocrine to immunological, infectious and genetic factors.

Pharmaceutical research and development relating to IDDM has concentrated on developing 'purer' and more effective forms of insulin and new delivery methods designed to achieve better control of blood sugar levels in the hope of reducing long term complications. Insulin pumps for continuous subcutaneous infusion delivery have been developed, though they have failed to live up to their original promise – at least for widespread use. The more recent refinement of insulin injection devices now offers many patients with diabetes a convenient means of frequent and flexible medication. In the mid eighties genetically engineered human insulin was introduced and in many countries it is now being substituted for insulin of animal origin.

For NIDDM, oral hypoglycaemic agents were first introduced in Germany in 1955. These have been extensively developed and there are now some hundreds on the market worldwide. Of the two broad classes, the sulphonylureas act mainly by stimulating release of insulin from the beta cells in the pancreas. Though the mode of action of the biguanides is controversial, they are believed to increase the peripheral uptake of glucose.

Aside from drug therapy, diet has been the mainstay of diabetes management. An interesting and profound observation on the effect of environment on the incidence and progression of diabetes was made by the French physician Bouchardat in 1875 during the prolonged Prussian siege of Paris. As food supplies dwindled and his fellow citizens were forced to eat rats, dogs and cats to survive, he noted that new cases of diabetes had ceased to appear in his practice and that the symptoms of those who had diabetes were much alleviated. In World Wars I and II similar observations were made and it was further noted that national death rates for diabetes fell markedly during these years of conflict and deprivation[3]. The importance of dietary modification in the treatment of diabetes has long been recognised, but exactly what diet has been a matter of debate which culminated in a reversal of earlier recommendations in most countries in the late seventies and early eighties. Whereas previously patients with diabetes had been advised to follow a restricted carbohydrate diet (implying a diet high in fat), they are now advised to follow a regime based on energy regulation (and restriction if they are overweight) in which intake is low in fat and high in unrefined carbohydrates and dietary fibre. Thus dietary advice in diabetes is directed not only at blood glucose control but also at the prevention of cardiovascular disease. It is broadly the same advice as that offered to the general population by a number of recent expert committees on nutrition.

3 It is noted that while there is evidence that starvation reduces the incidence of diabetes, there is a separate type of diabetes related to malnutrition (see Table 2).

Classification of diabetes

Diabetes is not now regarded as a single disease but as a group of syndromes with common biochemical features, of which an elevated blood glucose is the most evident, and which share several symptoms, signs and complications. The World Health Organisation has now adopted the IDDM and NIDDM nomenclature to describe the two main

Table 2 **Characteristics of the main subcategories of diabetes mellitus**

Insulin dependent diabetes mellitus (IDDM)	*Non-insulin dependent diabetes mellitus (NIDDM)*	
	Majority of NIDDM	Maturity onset diabetes in the young (MODY)
*symptoms frequently present at diagnosis – thirst, polyuria, polydipsia, weight loss	*often symptom free at presentation	*rare
*clearly elevated blood glucose levels	*may need OGTT for diagnosis	*autosomal dominant inheritance
*tendency to ketoacidosis and coma	*no tendency to ketoacidosis	*infrequent requirement for exogenous insulin
*complications develop in many cases – retinopathy, neuropathy, nephropathy and peripheral vascular disease	*similar complications as in IDDM but nephropathy is less common	*freedom from complications in most cases

Malnutrition Related Diabetes Mellitus (MRDM)	
Fibrocalculous pancreatic diabetes	*Protein-deficient pancreatic diabetes*
*fibrosis and stone formation in pancreas *requirement for insulin *resistence to ketoacidosis *distribution largely confined to tropical countries	*no pancreatic fibrosis *requirement for insulin resistence to ketoacidosis *distribution largely confined to tropical tropical countries

categories (WHO, 1985). The terms type 1 and type 2 diabetes are still used frequently by clinicians and immunologists but, after being advocated in an earlier WHO Report (Expert Committee Report No 646) as synonyms for IDDM and NIDDM, they are now no longer supported by WHO. Superimposed on the IDDM/NIDDM classification is another important entity – malnutrition related diabetes mellitus (MRDM) – which usually requires insulin treatment and is largely restricted to tropical countries. The principal features of each type of diabetes are set out in Table 2. The recently introduced category of Impaired Glucose Tolerance (IGT – see below) is best considered as a separate syndrome and has not been included in the Table.

It may seem confusing that the IDDM and NIDDM dichotomy refers to *dependency* on injected insulin, not to *treatment* with insulin. At any one time, a proportion of patients with NIDDM will be receiving insulin as one of a number of alternative therapies for their condition. Conversely, a small number of IDDM patients may *not* be receiving insulin, perhaps because they are in the so-called 'honeymoon phase' of their disease. This occurs in some cases shortly after diagnosis when pancreatic function is temporarily regained to the extent that exogenous insulin treatment becomes unnecessary. This is a short lived phenomenon and all true IDDM subjects will be treated with insulin for most, if not all, of their diabetic lives.

IDDM

Diagnosis and treatment of IDDM

'Acute diabetes', 'juvenile onset diabetes' and 'juvenile onset type diabetes' were the terms previously in common usage for what is now called IDDM. These terms reflect some of the clinical characteristics of the disease that have become well known to physicians. IDDM frequently has a sudden onset, though in many cases immunological processes associated with the disease can be identified some years before symptoms arise and, without insulin treatment, ketoacidosis, coma and death can result. It is the commonest form of the disease encountered in childhood and adolescence though IDDM is by no means confined to early life.

The diagnosis of IDDM is usually straightforward. The patient usually has symptoms (thirst, weight loss, malaise and the passing of large quantities of urine) and the blood glucose is raised. The presence of symptoms and one blood glucose value (on a casual sample) which is clearly in the abnormal range (>=11.1 mmol/l venous plasma or >=12.2 mmol/l capillary plasma) are enough to make the diagnosis.

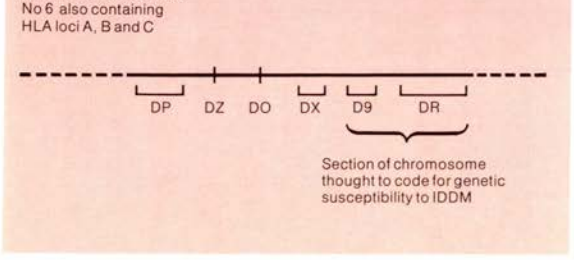
After diagnosis, elevated blood glucose levels will need to be treated during a period of stabilisation and the patient and his or her family will need a period of education and behaviour modification. In most industrialised countries, until recently, it was usual to admit new IDDM patients to hospital for this stabilisation and education. The development of diabetes centres and the involvement of the diabetes specialist

nurse as part of the clinical team have meant that these are frequently carried out without admission, either in centres or at home. During this period, patient and family need to master the techniques of insulin injection, the principles of dietary therapy, blood and urine testing and a number of other important aspects of the life of the person with diabetes.

Insulin therapy will mean at least daily subcutaneous injections, though it is more usual for two or three injections per day to be recommended. This, combined with the monitoring of urine or, more usually, blood glucose levels can keep most people with IDDM symptom free and out of danger of both ketoacidosis and clinical hypoclycaemia for most of the time but it rarely keeps blood glucose levels within the normal physiological range. Control of blood glucose is regarded as particularly important during pregnancy and close attention to insulin dosage, diet and blood glucose monitoring are frequently advocated in order to reduce the effect of maternal diabetes on the developing fetus.

Despite increasing sophistication in insulin treatment, long term complications (see below) are common in IDDM and life expectancy is considerably less than that of non-diabetic subjects (see *The Costs of Diabetes*, below). The disease may affect the eyes, kidneys and nerves, the blood supply to the legs and feet and the major blood vessels of the body. As a result, patients may suffer impairment of vision or even complete blindness, renal failure, peripheral or autonomic neuropathy and foot ulceration, gangrene and heart disease. One common factor in this panoply of pathological processes may be the progressive thickening of capillary basement membranes as a result of elevated blood glucose.

Figure 1 **Human histocompatibility system determining genetic predisposition to IDDM – the DR and DQ loci**



Adapted from Todd J A, Bell J I and McDevitt H O *HLA-DQB gene contributes to susceptibility and resistance to insulin-dependent diabetes mellitus*. Nature (1987) *329*, 599–604.

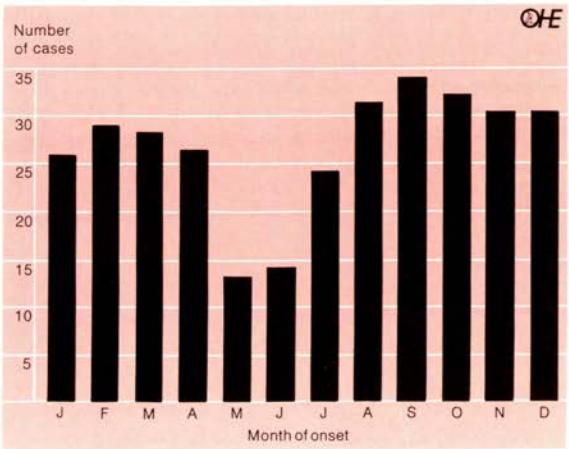
The causes of IDDM

IDDM shows clear population associations with certain recognised genetic markers in the same chromosomal region as the HLA (human leucocyte antigen) system which is part of the histocompatibility system, Figure 1. The disease is known to cluster in families and to be transmitted along with certain HLA haptotypes. Geographic and ethnic variations in incidence have been described, part of which may be genetically determined. Environmental factors are also important, however, and it may well be that infective agents, particularly viruses, are the environmental triggers which lead to the onset of the disease in genetically susceptible individuals. The pathogenesis of the disease is via immunological damage to the pancreatic beta cells. Epidemiological observations which have suggested the importance of environmental factors are:

(i) Seasonal variations in incidence which are consistent from year to year and seen in many parts of the world. There are higher incidence rates in autumn and winter months than in spring and summer months, Figure 2.

(ii) Age related incidence peaks at around the fifth and twelfth birthdays – times at which children encounter new environmental influences as they enter full time schooling and change schools.

Figure 2 **Seasonal fluctuation of month of onset in 317 cases of 'acute diabetes'**



Data from Adams S A *The seasonal variation in the onset of acute diabetes.* Arch Intern Med (1926) 37, 861–864.

(iii) Case control studies which have shown rising titres to viral antigens more often in the case of IDDM than in controls.

(iv) Secular increases in IDDM incidence in some countries which are relatively short term and cannot be explained by changes in genetic susceptibility.

(v) Animal experiments which show that a pathological state indistinguishable from human IDDM can be produced in genetically susceptible mice through infections with viruses, among them coxsackie B4.

(vi) A small number of intensively reported cases of individuals who die in diabetic ketoacidosis soon after onset of diabetes and whose pancreatic tissue shows infiltration by lymphocytes.

NIDDM

Diagnosis and treatment

The terms 'maturity onset diabetes' and 'mild diabetes' have been applied to NIDDM in the past. The former reflects the fact that NIDDM is uncommon below the age of 35 years. The second of these terms – 'mild diabetes' – is dangerously misleading because, although it is true that the dramatic, immediate manifestation of ketoacidosis is not part of NIDDM, the long-term sequelae of the disease are similar to those of IDDM and equally devastating in terms of their effects on the health and well-being of individuals.

NIDDM, in contrast to IDDM, is frequently discovered in a symptom free patient presenting for routine medical examination. Many newly diagnosed NIDDM patients are overweight. Its onset may be accompanied by symptoms of thirst, polyuria and malaise, though these are likely to be relatively mild. Diagnosis is either by means of a raised casual blood glucose or, if this is equivocal, by means of an Oral Glucose Tolerance Test (OGTT). The diagnostic values currently taken as indicative of diabetes and impaired glucose tolerance are given in Table 3.

The first line of treatment of NIDDM, especially if the patient is overweight at diagnosis, is energy restriction and a diet high in unrefined carbohydrate and low in fat. If this leads to significant weight loss, any symptoms, signs and often the biochemical abnormalities of the disease will be reduced and may even by eliminated.

As a second line of treatment, a combination of dietary therapy and oral hypoglycaemic agents will be considered. Failure of this approach to produce satisfactory control of blood glucose may lead to the commencement of insulin therapy. There are considerable differences between physicians in their approach to the treatment of NIDDM, and from country to country (Fontbonne *et al*, 1986). In France, for example, fewer NIDDM patients are treated with insulin than in many other European countries, while the prescription of oral hypoglaemic agents is correspondingly higher, and rising. Short-term treatment with insulin may be essential or at least highly desirable in NIDDM patients for example at times of infection or to achieve effective control of hyperglycaemia during surgical treatment.

Table 3 **Diagnostic values for the oral glucose tolerance test**

	Glucose concentration, mmol/litre (mg/dl)			
	Whole blood		*Plasma*	
	Venous	*Capillary*	*Venous*	*Capillary*
Diabetes mellitus				
Fasting value	⩾6.7 (⩾120)	⩾6.7 (⩾120)	⩾7.8 (⩾140)	⩾7.8 (⩾140)
2 hours after glucose load*	⩾10.0 (⩾180)	⩾11.1 (⩾200)	⩾11.1 (⩾200)	⩾12.2 (⩾200)
Impaired glucose tolerance				
Fasting value	<6.7 (<120)	<6.7 (<120)	<7.8 (<140)	<7.8 (<140)
2 hours after glucose load*	6.7–10.0 (120–180)	7.8–11.1 (140–200)	7.8–11.1 (14–200)	8.9–12.2 (160–220)

*For epidemiological or population screening purposes the 2-hour value after 75 g oral glucose may be used alone or with the fasting value. The fasting value alone is considered less reliable since true fasting cannot be assured and spurious diagnosis of diabetes may more readily occur.

Source Adapted from WHO Technical Report 727.

The causes of NIDDM

As with IDDM, the factors concerned with the development of NIDDM are partly genetic and partly environmental. The fact that the concordance rate for NIDDM in identical twins approaches 100 per cent (whereas that for IDDM is more like 45 per cent) suggests that genetic factors are strongly influential in the former, though clearly the frequency with which environmental triggers for NIDDM are encountered is a possible factor in the concordance between twins. It is known that, wherever the genetic factors for NIDDM are in the genome, they are not closely linked to the histocompatability genes as are those which influence the development of IDDM. In fact, no convincing genetic marker has yet been described for this form of diabetes.

The very high prevalence recorded for NIDDM in populations that have recently undergone a transition from hunter-gathering to a settled urban existence, such as the Pima Indians of Arizona, the Nauruan Islanders and the Australian Aborigines, has led to the suggestion that the genetic predisposition to NIDDM was, at one time, of survivial advantage in human groups. This 'thrifty genotype' hypothesis (Neel, 1962) further suggests that the predisposition to NIDDM only became a disadvantage when the lifestyle of these groups changed from one of high physical activity with a diet high in unrefined carbohydrate and low in fat to one in which there was less emphasis on physical activity and in which dietary intake was high in refined carbohydrate and fat. In several Third World countries, the prevalence of both obesity and NIDDM among the adult population may be as much as 30-35 per cent (see

below) and this has severe consequences on mortality and morbidity.

Environmental influences on the development of NIDDM almost certainly include diet though no specific dietary components – fat, protein, carbohydrate, vitamins, trace elements or dietary fibre – have been convincingly implicated either by physiological or by epidemiological studies. It is more likely that the energy content of the diet, in relation to physical energy expenditure, acting through body mass and obesity, is a potent influence though this cannot be the whole explanation since some NIDDM patients are not obese at the time of diagnosis. Even so, in comparisons between populations, dietary factors related to energy intake and levels of obesity or body mass in the population explain a considerable proportion of the observed variation.

Malnutrition related diabetes

Malnutrition related diabetes mellitus (MRDM) as presently defined includes the varieties of diabetes known in the past as tropical diabetes, pancreatic diabetes, endocrine pancreatic syndrome and ketosis-resistant diabetes for the young. A recent monograph on MRDM (Bajaj *et al*, 1984) suggests two main subclasses – fibrocalculous pancreatic diabetes and protein-deficient pancreatic diabetes.

Fibrocalculous pancreatic diabetes is characterised by fibrosis of the pancreas and stone formation in the main pancreatic duct and branches. Most patients with this disease are under 30 years of age at diagnosis and tend to be underweight and require insulin but are not prone to ketoacidosis. Toxins derived from cassava and other cereal foods have been implicated in its causation. It is commonest in tropical African and West Indian countries and in India, Bangladesh and Sri Lanka.

Protein-deficient pancreatic diabetes is similarly a desease of the younger inhabitants (under 35 years of age) of tropical countries. It also requires insulin for treatment and patients, again, are not prone to the development of ketoacidosis. They, like those with fibracalculous disease, show weight loss and other characteristics of malnutrition before diagnosis but there is no pancreatic calcification and fibrosis. This variety of MRDM was previously called J-type or M-type diabetes, malnutrition diabetes or ketosis-resistant youth-onset diabetes.

Maturity onset diabetes in the young – MODY

There is a further subcategory of diabetes which, though probably rare, is of considerable interest from the clinical and genetic point of view. This is usually known as Maturity Onset Diabetes in the Young (or MODY) and its characteristics are: early onset (usually before 35 years of age), lack of dependence on injected insulin (usually treated by diet alone or by oral hypoglycaemics), a dominant pattern of inheritance within families (half of the siblings affected on average and, usually, one parent) and relative freedom from the complications usually seen in other forms of diabetes. MODY may be a genetically distinct subtype of NIDDM.

This variety of diabetes was first described in the patients attending King's College Hospital Diabetic Clinic in south London. A small number

of families could be identified (one such was the Mason family – hence the synonym 'Mason-type diabetes') in which diabetes was longstanding, autosomal dominant inheritance seemed likely and the affected members were free of diabetic complications. MODY probably constitutes a very small proportion of NIDDM patients.

Impaired glucose tolerance

The category of Impaired Glucose Tolerance (IGT) was introduced by the US National Diabetes Data Group (1979) and later endorsed by the WHO Expert Committee Report No 646 (WHO 1980). Hitherto, the term 'borderline diabetes' had been used for those whose glucose tolerance was 'impaired' compared with that of clearly non-diabetic people, but who were not categorised as frankly diabetic. The IGT category was introduced partly to take away the label of 'diabetes' from these individuals, a label which is inappropriate since this level of glucose intolerance is not associated with development of the microvascular complications of diabetes (retinopathy, nephropathy, etc). IGT is, however, associated with an increased risk of death from ischaemic heart disease.

People with IGT are not necessarily at an intermediate stage between normal tolerance and diabetes, though an undetermined proportion of them do progress to diabetes within a few years. Exactly how many is not known. Estimates range from about 1 per cent to 5 per cent of the IGT population per year though this clearly depends on the age of the subjects studied and, because of this relationship with age, the duration of follow up. In the Bedford survey, 15 per cent of those classified as having IGT at the outset had progressed to diabetes after 10 years (Keen *et al.* 1982). Other studies of progression from IGT to frank diabetes, such as that of Whitehall Civil Servants (Jarrett *et al.* 1979) and King *et al's* (1984) study of the Micronesian population of Nauru, differ in their estimates of the risk of progression and differ also in the extent to which body mass, the level of blood glucose at baseline testing and other characteristics are predictors of risk. Studies are under way in several countries to determine whether treatment of IGT (by dietary modification, for example) can restore normal glucose tolerance, reduce the risk of progression to frank diabetes and reduce mortality from ischaemic heart disease.

Complications of diabetes

Most of the mortality, morbidity and costs of diabetes arise from its long-term complications and sequelae rather than its acute episodes. This is true for both major sub-types of the disease, where the pathological processes involved in the development of complications, *eg* thickening of capillary basement membranes, are the same. NIDDM patients are probably no less liable to the development of retinal, renal, neurological and vascular complications than IDDM patients given equal duration of disease but, since IDDM is more likely to have commenced during childhood, adolescence or early adulthood, duration of disease in NIDDM is usually shorter than in IDDM. Perhaps because of this, nephropathy and end stage renal failure are seen less frequently in NIDDM than in IDDM patients.

Cardiovascular Disease

Cardiovascular disease is the major cause of death and hospitalisation among people with diabetes. The incidence and prevalence of ischaemic heart disease in patients with diabetes has been investigated by several large international studies. Only a minority of these studies have drawn the distinction between IDDM and NIDDM. Nevertheless, it seems likely that there is a substantial excess risk of heart disease in both of the major types of diabetes (see *The Costs of Diabetes*, below).

Several risk factors for ischaemic heart disease, in diabetic and non-diabetic subjects, are now well established. These include the three major risk factors of elevated serum cholesterol, hypertension and cigarette smoking, as well as the 'minor' risk factors of positive family history, a predominantly central deposition of fat and so on. The excess mortality observed in diabetic patients is not fully explained by higher levels of these known risk factors, though it is true, for example, that the prevalence of hypertension is usually higher in patients with diabetes than in age-matched controls (Diabetes Drafting Group, 1985).

The prevention of ischaemic heart disease in diabetes is partly related to the prevention of diabetes, partly to reducing the levels of known risk factors such as cigarette smoking and, perhaps, partly to modifying hyperinsulinaemia and coagulation disorders in patients who already have diabetes. While the first and third of these strategies are still distant prospects, the second is theoretically possible now – though seemingly as difficult to achieve in the diabetic as in the non-diabetic population.

Follow up data from the Framingham Study (Abbott *et al*, 1988) show that cardiac failure is a common occurence among diabetic patients who survive a myocardial infarction, warranting early detection and vigorous management in convalescence. Where cardiac failure appears, control of diabetes assumes added importance, particularly in women, where its effect on survival is considerable.

Nephropathy

Nephropathy is a serious complication which is more common in IDDM than in NIDDM. Its first clinical manifestation is the presence of a protein, albumin, in the urine. Deterioration of kidney function progresses at a variable rate, leading to end stage renal failure if death does not intervene first. The cause of diabetic nephropathy remains unknown and there is no known means of prevention. Recent research, however, offers some prospect of arresting the decline of kidney function through improved glycaemic control or, in the case of hypertensive IDDM patients, through medication with ACE (angiotensin converting enzyme) inhibitors (Bjorck *et al*, 1986).

Neuropathy

Neuropathy is a debilitating complication of diabetes which may be very common (see *Epidemiology*, below) though problems with standardisation of methods have made the estimation of incidence and prevalence very difficult. Risk factors, also, are poorly understood, and effective means of prevention and treatment are limited. Peripheral neuropathy

is associated with pain, parasthesiae, hyperasthesiae as well as numbness and other symptoms. The commonest problem arising from diabetic neuropathy is reduced sensation in the feet which can rapidly lead to ulceration. This is often associated with vascular insufficiency and the eventual treatment is often amputation. Prevention is largely focussed at present on patient education and foot care (in particular the early identification of minor injuries likely to give trouble if left untreated and the provision of suitable and correctly fitted footware). These preventive measures clearly depend on regular follow up of patients and on the availability of trained and motivated staff.

Retinopathy

Retinopathy, if not identified and treated early, may lead to significant visual loss and, eventually, to blindness. The incidence of blindness in IDDM patients is partly determined by duration of disease but also by quality of blood glucose control and blood pressure. In NIDDM, complications such as retinopathy may be present at the time of diagnosis, a reflection of the insidious clinical onset of the disease which may go undetected for some years. Serum lipid levels do not seem to contribute to the risk of retinopathy and the evidence for cigarette smoking as a risk factor is equivocal. Several studies support the view that the quality of glycaemic control is an important factor in delaying the occurrence and slowing the development of retinopathy in IDDM and there is a general recognition that in all diabetic patients the early detection and treatment of diabetic retinopathy is crucial for the prevention of visual impairment.

Epidemiology

International variations in IDDM

Recently summarised incidence data taken from registers of childhood IDDM exhibit a fifty-fold variation between countries (Rewers *et al*, 1988). The highest rate has been recorded in Finland, with just under 30 new cases per 100,000 inhabitants per year in the 0-14 year age group. Far eastern countries are amongst those with the lowest recorded incidences, 1.7 per 100,000 inhabitants per year in Japan and 0.6 per 100,000 in Korea, Table 4. Incidence rates in northern Europe tend to be higher than those in southern Europe though this North/South gradient is not as clear in North America and elsewhere.

The estimation of incidence rates from population registers is, however, not without difficulty. To be valid, a number of conditions have to be satisfied:

- common definitions of IDDM
- ascertainment of *all* new cases occurring within a defined population over a defined period of time
- accurate enumeration of the population at risk at the mid point of the period of observation

It is likely that a number of the registries included by Rewers *et al* do not entirely satisfy these criteria. Thus the suggestion of a North/South gradient in incidence should not be accepted at face value. There is little doubt, however, that there are large differences in incidence between Europe and America on the one hand and, on the other, Eastern countries such as Japan, Hong Kong and, possibly, the People's Republic of China (Yan *et al*, 1982).

The reasons for the East/West differences remain obscure. Anthropological studies have revealed large differences in the population frequencies of certain HLA antigens, including those associated with IDDM. Although many of the associations are similar in European and Japanese populations, the frequency of many of the marker genes are lower in the Japanese. Migrant studies which might help to disentangle influence of heredity and environment have not been carried out in IDDM to anything like the same extent as in cardiovascular disease and cancer. Such work as has been done, for example on French children in France and Canada (Colle *et al*, 1981 and Hours *et al*, 1984) is not wholly convincing.

Sex differences

Comparisons of the relative incidences of IDDM in boys and girls in high and low incidence populations suggest that, although the incidence in boys is higher than that in girls in high incidence populations, it is usually the female incidence rates which are higher where IDDM as a whole is rare. Indeed, in some 'low incidence' populations, the female incidence is not significantly lower than that in populations which are regarded as 'high incidence' populations, Table 5. The reasons for these sex differences in incidences are not known.

Changes in IDDM incidence rates

Whether or not there have been real changes in the frequency of diabetes is an intriguing and important question, not only because of the impact on health service resources, but because of the clues that hard epidemiological data would give to the causes of diabetes. Reports from a number of countries, particularly in northern Europe, have indicated sustained increases in incidence and prevalence over recent decades which are suggestive of an environmental factor or factors which either causes diabetes or triggers it in susceptible individuals. If identified, knowledge of such factors might lead the way to prevention. Nearly all the data that are available worldwide relate to IDDM among young people, where trends in incidence are considerably easier to document than for NIDDM.

In a review by Bingley and Gale (1989a) the hardest evidence of an increase in IDDM incidence comes from Finland, Poland and the Netherlands. Studies in the United States have failed to demonstrate any significant increase in IDDM over time.

In Finland, the national drug register provides accurate data with estimated ascertainment of over 95 per cent and new cases of IDDM among people under 20 years of age rose from 27 cases per 100,000 population

Table 4 **Age-standardized incidence rates of insulin-dependent diabetes mellitus under age 15 years (per 100,000 population) and the 95 per cent confidence intervals, 1965–1986**

Region *Country and area*	*Study period*	*Estimate of ascertainment*	*Incidence per 100,000*					
			M	*(Cases)*	*95% CI*	*F*	*(Cases)*	*95% CI*
AMERICAS								
Canada								
Montreal	1971–85	94%	9.6	(461)	8.8–10.5	10.0	(458)	9.1–11.0
Prince Edward Island	1975–86	99%	27.0	(53)	20.4–35.6	20.8	(39)	14.8–28.4
Cuba	1978–80	?	2.5	(128)	2.1–3.0	2.8	(139)	2.4–3.3
Mexico								
Mexico City	1984–86	?	0.4	(38)	0.3–0.5	0.7	(62)	0.5–0.9
United States								
Allegheny County	1965–85	>90%	15.1	(568)	13.9–16.4	16.0	(580)	14.7–17.4
Colorado	1978–83	>95%	14.8	(304)	13.2–16.6	15.2	(300)	13.5–17.1
Jefferson County	1979–85	96%	9.9	(52)	7.5–13.1	14.9	(76)	11.8–18.8
North Dakota	1980–86	?	21.6	(120)	18.0–25.9	16.2	(84)	13.0–20.2
Rochester	1965–79	100%	15.8	(18)	9.4–25.0	18.4	(20)	11.2–28.3
San Diego	1978–81	?	9.6	(25)	6.2–14.2	9.1	(23)	5.8–13.7
Wisconsin (part)	1970–79	>90%	20.2	(94)	16.4–24.8	16.2	(72)	12.8–20.5
ASIA								
Israel	1975–80	?	4.4	(142)	3.7–5.2	4.6	(154)	3.9–5.4
Japan								
Hokkaido	1974–86	≅ 100%	1.3	(112)	1.1–1.6	2.1	(171)	1.8–2.3
Kuwait	1980–81	?	3.2	(9)	1.5–6.1	4.7	(13)	2.4–8.2
Republic of Korea	1985–86	?	0.5	(17)	0.3–0.9	0.6	(18)	0.4–1.0

EUROPE								
Austria[a]	1979–86	93%	8.0	(431)	7.3–8.8	7.3	(379)	6.6–8.1
Denmark (part)	1970–76	88–99%	14.5	—	—	13.4	—	—
Finland	1970–86	99%	30.4	(2,684)	29.3–31.6	27.1	(2,292)	26.0–28.2
France								
Département du Rhône	1960–79	>90%	4.6	(155)	3.9–5.4	4.9	(159)	4.2–5.7
German Dem Rep	1982–84	?	7.0	(340)	6.3–7.8	7.0	(327)	6.3–7.8
Netherlands	1978–80	90%	9.9	(500)	9.1–10.8	9.6	(465)	8.8–10.5
Norway	1973–82	92%	21.4	(1,039)	20.1–22.7	19.4	(890)	18.2–20.7
Poland								
Warsaw	1984–86	?	5.2	(16)	3.0–8.4	5.5	(16)	3.1–8.9
Wielkopoiska	1970–85	96%	4.7	(238)	4.1–5.3	4.9	(235)	4.3–5.6
Sweden	1978–86	93%	23.8	(1,747)	22.7–24.9	22.5	(1,571)	21.4–23.6
United Kingdom								
Leicestershire	1965–81	>90%	8.7	(140)	7.3–10.3	8.6	(132)	7.2–10.2
Scotland	1976–83	≧ 100%	20.0	(966)	18.8–21.3	19.4	(890)	18.2–20.7
Tayside	1980–83	≧ 100%	19.7	(36)	11.0–32.5	22.1	(28)	12.6–35.8
OCEANIA								
New Zealand[b]	1968–72	?	8.6	(212)	7.5–9.9	9.1	(216)	7.9–10.4
Auckland	1978–85	?	9.0	(109)	7.4–10.9	10.5	(124)	8.8–12.5
Canterbury	1982–85	≧ 100%	10.2	(18)	6.0–16.1	12.9	(21)	8.0–19.7

a Age group 0–13 years.
b Age group 0–15 years.

Source Rewers *et al* (1988) World Health Statistics Quarterly *41*, 179–189.

Table 5 **Age-standardized incidence of insulin-dependent diabetes mellitus under age 15 years (per 100,000 population) and the 95 per cent confidence intervals, by ethnic groups**

	Incidence per 100,000					
Area, ethnic group	*M*	*(Cases)*	*95% CI*	*F*	*(Cases)*	*95% CI*
Allegheny County						
white	16.1	(530)	14.8–17.5	16.4	(520)	15.0–17.9
black	8.3	(38)	5.9–11.4	13.2	(60)	10.2–17.1
Colorado						
non-Hispanic	16.4	(282)	17.3–18.5	15.9	(260)	14.1–18.0
Hispanic	6.6	(22)	4.1–10.0	12.3	(40)	8.8–16.7
Jefferson County						
white	15.5	(48)	11.4–20.6	18.1	(54)	13.7–23.8
black	1.9	(4)	0.5–4.9	10.4	(22)	6.5–15.7
Auckland						
white	12.1	(103)	9.9–14.7	12.8	(110)	10.6–15.5
Maori and Polynesian	2.0	(6)	0.7–4.4	4.9	(14)	2.7–8.2
Montreal						
French	7.9	(249)	7.0–9.0	8.1	(242)	7.1–9.2
British	15.4	(86)	12.4–19.1	16.9	(90)	13.7–20.9
Italian	9.8	(28)	6.5–14.2	9.5	(26)	6.2–14.0
Jewish	14.1	(19)	8.5–22.0	22.5	(29)	15.1–32.4
other	12.8	(79)	10.2–16.0	12.2	(72)	9.6–15.5

Source Rewers *et al* (1988) World Health Statistics Quarterly *41*, 179–199.

in 1970–76 to 38 per 100,000 in 1983, over a period in which the method of ascertainment was unchanged (Åkerblom and Reunanen, 1985). In Poland, there has been a recent report of an apparent epidemic of IDDM with incidence rising from 3.5 per 100,000 population below 17 in 1970–81 to 6.6 per 100,000 in 1982–4 (Rewers *et al*, 1987). Most striking of all, Bingley and Gale quote data on conscripts to the Royal Dutch Army, showing a steady increase in prevalence of IDDM, as determined on medical examination, from 0.99 per 1000 in 1960–64 to 1.98 per 1000 in 1985/8.

International variations in NIDDM

Prevalence and incidence of NIDDM are not as well-documented throughout the world as IDDM. Broadly, however, populations may be divided into four groups:

1 those which have a very low prevalence of NIDDM (under 1 per cent). Examples of such populations are rural Melanesian groups living according to their traditional lifestyle (*eg* Papuan New Guinea highlanders and Solomon Islanders), Eskimo groups before urban settlement and rural Bantu populations.

2 those with low prevalences, from 1 per cent to 10 per cent. In this group are most European and North American populations including the United Kingdom, North American, Australian, New Zealand and South African populations of European origin and Bantu groups recently urbanised which are probably undergoing a transition from close to zero prevalences.

3 populations with NIDDM prevalence rates between 10 per cent and 20 per cent. Such populations include Singapore and South African residents of Indian origin, rural Indians in India, and Australian Aborigines.

4 a small number of the world's populations show markedly high prevalence rates for NIDDM (that is, over 20 per cent). Well documented examples are Pima and other North American Indian groups (Pima men aged over 20 years have a prevalence of 33 per cent, women of the same age range 37 per cent) and inhabitants of the Island of Nauru (Micronesia). The latter (adults aged over 20 years) have a reported prevalence of 25 per cent (men) and 24 per cent (women).

Since the great majority of prevalent cases of diabetes are NIDDM, total diabetes prevalence can be taken as a fairly good proxy for NIDDM. Britain, with its estimated prevalence of something over 1 per cent occupies a fairly low position in the second of the above groups. Prevalence in the United States is substantially higher, though exactly how much higher is a matter of dispute. Thus one recent, well designed study, the 'Three City Study' of Minnesota (Bender *et al.* 1986) has reported the prevalence of *clinically detected* NIDDM and IDDM combined at 1.6 per cent, age-standardized to the 1970 US Caucasian population. In contrast, diagnosed diabetes was reported by 2.5 per cent of the sample of Americans interviewed in the 1981 National Health Interview Survey (Harris, 1985).

There is also disagreement on trends over time. The National Health Interview Surveys show a secular rising trend in crude diabetes preva-

Table 6 **Diabetes sales and diagnoses data, 1988**

	Total Antidiabetics		*Insulin*	*Oral Antidiab.*	*Diagnosis*
	Sales $ million	% of Pharma Sales	% of Pharma Sales	*% of Pharma Sales*	% of all Diagnoses
Canada	45	1.7%	1.0%	0.7%	2.0%
France	110	1.4%	0.4%	1.0%	2.6%
Germany	210	2.1%	1.4%	0.7%	1.9%
Italy	85	1.1%	0.6%	0.5%	3.0%
Japan	140	0.6%	0.3%	0.3%	2.5%
UK	75	1.8%	1.3%	0.5%	1.4%
USA	675	2.3%	1.3%	1.0%	3.0%

Source Squibb Estimates.

Table 7 **Age specific prevalence of known diabetes per 1,000 population**

	Oxford			*Poole*			*Southall*		
Age	*Population*	*Diabetics*	*Prevalence*	*Population*	*Diabetics*	*Prevalence*	*Population*	*Diabetics*	*Prevalence*
0–9	4,252	2	0.5	10,882	6	0.6	2,620	0	—
10–19	5,954	6	1.0	13,452	32	2.4	4,155	5	1.2
20–29	6,772	26	3.8	11,300	48	4.2	3,775	14	3.7
30–39	5,411	34	6.3	13,755	56	4.1	3,195	14	4.4
40–49	4,476	32	7.1	10,723	82	7.7	3,030	23	7.6
50–59	4,696	74	15.8	9,839	127	12.9	3,625	48	13.2
60–69	4,080	90	22.1	9,970	200	20.1	3,205	76	23.7
70–79	3,107	131	42.2	7,645	270	35.3	2,510	93	37.1
80+	1,331	38	28.6	3,002	96	32.0	865	51	59.0
Total	40,079	431	—	90,660 [b]	917	—	26,980	324	—
Crude prevalence		10.8 (9.7–11.8)			10.1 (9.5–10.7)			12.0 (10.7–13.3)	
Age-adjusted prevalence[a]		10.4 (9.4–11.4)			9.5 (8.9–10.2)			10.5 (9.3–11.8)	

[a] Directly standardized to 1981 population of England and Wales.
[b] Excluded 92 persons: age unknown.
95% confidence intervals are stated in parenthesis.

Source Neil *et al* (1987) The Oxford Community Diabetes Study. *Diabetic Medicine* 4: 539–543.

lence, from 0.4 per cent in 1935/6 to 2.5 per cent 1979–81. Bender *et al* (1986), in contrast, maintain that many of the population studies carried out over this period show remarkably similar rates when they are age standardized and that claims that diabetes prevalence is rising in the United States should be treated with caution.

The frequency of diabetes as a diagnosis in primary care physician contacts gives another crude indication of variations in developed countries, though these may owe as much to differing medical traditions as to underlying levels of prevalence. Table 6.

The burden of NIDDM is of an altogether different magnitude in the third world, where in several countries the prevalence of both obesity and NIDDM may be as high as 30-35 per cent of the adult population.

International variations in impaired glucose tolerance

As a relatively new epidemiological concept, IGT has been studied in only a few populations. Its prevalence in American Blacks is around 10-15 per cent. Surveys in rural Italy and Australia (studying Australians of European origin) have suggested rates of 4 per cent or 5 per cent. IGT was present in New Guinea Islanders (though very rare) despite the absence of NIDDM.

Prevalence and incidence of diabetes in Britain

The combined prevalence of diagnosed IDDM and NIDDM is rather more than 1 per cent of the white British population. This implies between 500,000 and 750,000 people with clinically diagnosed diabetes in Britain. Allowing for undiagnosed people with diabetes may bring the total to 1 million or even more.

Five out of the six substantial, population based prevalence studies carried out in the nineteen-eighties in Britain are in broad agreement on this percentage. The results from three of them – carried out in Oxford (Neil *et al*, 1987), Poole (Gatling *et al*, 1985) and Southall (Mather *et al*, 1985) – are set out in Table 7. Observed prevalences are very close to each other at about 1 per cent of the study populations after standardisa-

Table 8 **Age – sex prevalence rates for diagnosed diabetes in Cambridgeshire**

Age	*Prevalence (%)*	
(y)	*Male*	*Female*
0–14	0.10	0.07
15–44	0.44	0.35
45–64	2.23	1.28
65+	4.50	4.12

Source Williams D R R (1985) Hospital admissions of diabetic patients: information from Hospital Activity Analysis. *Diabetic Medicine*, 2, 27–32.

tion to the 1981 age distribution for England and Wales. A fourth study, covering the population of three general practices in Cambridgeshire, gives a slightly higher prevalence of diagnosed diabetes of 1.2 per cent (Williams, 1985), but a very similar age distribution, Table 8. The remaining one of these five studies was carried out in a large general practice in Wales (Gibbins, Rowlands and Saunders, 1986). The authors found a prevalence of diabetes which was slightly higher again, at 1.36 per cent of the practice population, but gave no indication of the practice's age structure such as to allow comparison with the other surveys quoted.

The sixth study (Simmons, Williams and Powell, 1989) found a substantially higher prevalance of diagnosed diabetes among white people aged 20 or over in the Foleshill ward of Coventry, but much if not all of the difference may be explained by the socio-economic profile of the survey population, within a neighbourhood noted by the authors to be one of the most underprivileged wards in England and Wales. Though there is some evidence that IDDM occurs less frequently in children from working-class than middle-class backgrounds (Kurtz, Peckham and Ades, 1988) any such skew would be likely to disappear against the opposite social class gradient of the much more numerous group of people with NIDDM. The Coventry results confirm the positive association between poverty and high prevalence of diabetes (IDDM and NIDDM combined) reported by Barker, Gardner and Power (1982) in their study of nine British towns.

Each of these surveys of clinically diagnosed diabetes relied solely on inspection of medical records and no attempt was made to verify diagnostic criteria. This may have led to some overestimation, particularly in the light of more rigorous criteria which have been introduced since the surveys were undertaken. Conversely, there is likely to have been some degree of under-estimation from the exclusion of some people with confirmed diabetes, particularly those controlled by diet alone, as well as from under-representation of institutional populations, as specifically noted in the Oxford study.

Prevalence of IDDM and NIDDM in Britain

It is believed that about a quarter of people with diabetes in Britain have IDDM, but none of the major studies has satisfactorily distinguished the prevalence of IDDM from NIDDM in Britain. Thirty to forty per cent of the subjects with diabetes are treated with insulin according to major recent surveys, Table 9, but this includes an unknown number with NIDDM.

Incidence of IDDM and NIDDM in Britain

The best baseline information on the incidence of IDDM in Britain has recently been published by Bingley and Gale (1989b) for the entire Oxford health region. Using prospective registration of newly diagnosed cases, supplemented by hospital discharge records and death certificates and independently validated, they arrived at an estimated incidence of 15.6 cases of IDDM per 100,000 population aged under 21 per year. The

Table 9 **Age specific prevalence rate for known *insulin-treated* diabetes per 1,000 population**

	Oxford[b]			*Poole*[c]			*Southall*		
Age	*Insulin-treated patients*	% *Insulin-treated*	*Prevalence*[b]	*Insulin-treated patients*	% *Insulin-treated*	*Prevalence*	*Insulin-treated patients*	% *Insulin-treated*	*Prevalence*
0–9	2	100	0.5	6	100	0.5	0	—	—
10–19	6	100	1.0	32	100	2.4	5	100	1.2
20–29	11	91.7	3.5	44	91.7	3.9	13	92.9	3.4
30–39	18	85.7	5.4	44	78.6	3.2	9	64.3	2.8
40–49	10	40.0	2.9	42	51.2	3.9	10	43.5	3.3
50–59	21	38.9	6.1	47	37.6	4.8	19	39.6	5.2
60–69	17	25.4	5.6	55	28.1	5.6	14	18.4	4.4
70–79	20	20.8	8.8	61	23.2	8.2	18	19.4	7.2
80+	2	9.1	2.6	25	26.9	8.5	8	15.7	9.2
Total	107	—	—	356	—	—	96	—	—
Overall percentage insulin-treated		35.0			40.0			30.0	
Crude prevalence			3.8 (3.2–4.4)			4.0 (3.5–4.3)			3.6 (2.8–4.3)
Age-adjusted prevalence[a]			3.8 (3.2–4.4)			3.9 (3.5–4.2)			3.3 (2.6–4.0)

[a] Directly standardized to 1981 population of England and Wales.
[b] Treatment status available for 305 patients: prevalence rated adjusted proportionately.
[c] Treatment status available for 901 patients: prevalence rates adjusted proportionately.
95% confidence intervals are stated in parentheses.

Source Neil *et al* (1987) The Oxford Community Diabetis Study. *Diabetic Medicine* 4: 539–543.

Table 10 **Yearly incidence of insulin dependent diabetes mellitus during 1985–6 stratified by age and sex (cases 100,000)**

	Male population			*Female population*			*Total*		
Age group (years)	*No of cases*	*Incidence*	*95% Confidence interval*	*No of cases*	*Incidence*	*95% Confidence interval*	*No of cases*	*Incidence*	*95% Confidence interval*
0–4	11	6.5	2.7 to 10.3	9	5.6	2.0 to 9.3	20	6.1	3.4 to 8.7
5–9	31	19.0	12.3 to 25.7	15	9.8	4.8 to 14.8	46	14.6	10.3 to 18.8
10–14	46	26.5	18.8 to 34.1	43	26.3	18.4 to 34.1	89	26.4	20.9 to 31.8
15–19	36	16.0	10.8 to 21.2	33	16.5	10.9 to 22.2	69	16.2	12.4 to 20.1

Source Bingley P J and Gale E A M. Incidence of insulin dependent diabetes in England: a study in the Oxford region, 1985–6. Br Med J 1989; 298: 558–60.

highest incidence was in the 10-14 year age group at 26.4 per 100,000 per year (Table 10). These figures are about double those quoted from the British Diabetic Association register, a voluntary recording system which ran from 1972 to 1985 in which ascertainment was clearly incomplete. But they are consistent with the cumulative incidence estimates from the national child cohort studies cited below (see *Changes in Prevalence and Incidence of Diabetes*).

There is no information on the incidence of NIDDM in Britain, and very little on the overall annual incidence of IDDM and NIDDM combined. The best available data on the latter come from the mini-clinic population around Wolverhampton (Thorn 1983), where most new patients were seen at least once in the hospital clinic. This indicated an annual incidence of new cases of about 1.05 per 1,000 population, *ie* about one tenth of the combined IDDM and NIDDM prevalence.

Prevalence of undiagnosed diabetes

Wilkerson and Krall, 1947 – writing just after the second world war – estimated that half of all diabetes in the population was undiagnosed. This was confirmed in Britain by the Bedford study (Keen *et al*, 1982). It might be expected that a lower proportion of people with diabetes would be undiagnosed today, but the evidence is not entirely clear. The authors of the Coventry survey estimated that about 40 per cent of diabetes, as elicited by oral glucose tolerance testing, was undiagnosed in that socio-economically deprived population at the time of the survey in 1987, but the Islington survey (Forrest, Jackson and Yudkin, 1986) found that rather more than half of people with diabetes remained undiagnosed. A major question here is the extent to which these early unrecognised cases are developing the complications of diabetes.

Prevalence of Impaired Glucose Tolerance

Several features of IGT make it a particularly difficult subject for epidemiological study. These have been summarised by Jarrett (1987). IGT is an unstable state which may revert to normal or progress to frank diabetes. It lacks reproducibility in individuals and is also dependent on the age and sex composition of the population and other factors including, perhaps, adiposity. In the UK, the prevalence of IGT was found to be 0.94 per cent of subjects aged 21 and over in the Whitehall study and 1.5 per cent of people aged 40-64 in the Bedford study (Keen *et al*, 1982).

Changes in prevalence and incidence of diabetes

Some commentators have suggested there may have been an increase in recent decades in the overall prevalence of diabetes in Britain (IDDM and NIDDM combined), but the evidence is not convincing. Surveys of diagnosed diabetes carried out in Britain in the nineteen sixties include a major study of the Edinburgh population of almost half a million people (Falconer *et al*, 1971) and a smaller survey in Birmingham (Royal College of General Practitioners, 1962). They found prevalences of 6.3 per 1000 and 6.4 per 1000 respectively. This is about a third less than the Oxford, Poole and Southall surveys of the early eighties. However, it is not

known with any certainty whether the increase reflects under-ascertainment in earlier studies, improved clinical detection, an increase in incidence, a fall in mortality among people with diabetes or a combination of all these factors (Neil *et al*, 1987). It is known that mortality rates from coronary heart disease, to which people with diabetes are particularly vulnerable, have decreased slightly over the period. There has also been a substantial decrease in stroke and hypertension mortality, associated, in part, with the availability of effective anti-hypertensive therapy. But the impact of these improvements on the diabetic subgroup of the population is not known[4].

Incidence of IDDM is better documented than NIDDM. There are two sources of evidence for an increase in IDDM in Britain. One relates to increased rates of first admission to hospital for diabetes in the late 1960's and early 1970's among Scottish children. Patterson *et al* (1983) found an estimated 80 per cent increase in first admissions among children aged 0-18 throughout Scotland. Subsequent analysis of data up to 1983 found that diabetes admissions remained high, though the rising trend was no longer significant (Patterson *et al*, 1988). The method of estimation, however, was probably flawed. It involved assuming that all new cases of childhood diabetes were admitted to hospital during the period and that the ratio of new admissions to total admissions remained constant. Validation of the study methodology was later carried out in the Tayside region (Waugh, 1985) and a number of basic assumptions were found to be unjustified. The Scottish evidence for an increase in incidence of diabetes should probably, therefore, be discounted.

The most convincing data on changes in IDDM frequency in Britain come from three national birth cohort studies of children born in particular weeks in 1946, 1958 and 1970. Stewart-Brown *et al* (1983) found a significant increase in cumulative diabetes incidence for each of the three successive cohorts, rising from 0.01 per cent to 0.06 per cent and 0.13 per cent by the age of eleven years for those born in 1946, 1958 and 1970 respectively. More recently, however, Kurtz, Peckham and Ades (1988) have extended the analysis into the early twenties of the children in the 1946 and 1958 cohorts. They found that, by the age of 23, cumulative incidence of diabetes in the 1946 cohort had, at 0.45 per cent caught up with and surpassed that of the 1958 cohort, at 0.31 per cent, though the manner of presentation was markedly different in the two groups. Most of the later cases in the 1946 cohort were discovered among symptom free individuals at examination for military service or during pregnancy, in contrast with the 1958 and 1970 cohorts where first presentation was invariably symptomatic.

The authors suggest that the prevalence of IDDM among young people may not have increased in Britain, but may now be manifested at an earlier age, probably due to an as yet unidentified change in environmental factors. Similarly, Bingley and Gale, 1989a, in a recent review of incidence of IDDM in Europe, point out that the increase in childhood diabetes reported in various European countries could be due not to the

4 It is also suggested that NIDDM mothers have larger than average babies, and this may improve survival of those with a family history of diabetes.

disease becoming more common but to susceptible individuals becoming diabetic at an earlier age.

Ethnic variations in diabetes prevalence
Only the Coventry and Southall studies have looked specifically at variations in diabetes prevalence between white and ethnic minority populations in Britain. Both found that diabetes was about four times more common among people of Asian origin than among their white neighbours. The Southall study also reported separate data on people of Afro-Carribean origin, but found no difference in diabetes prevalence compared with the neighbouring white population.

Epidemiology of the complications of diabetes

Cardiovascular Disease
People with diabetes have a greatly increased risk of death from coronary artery disease and cerebrovascular disease (see *The Costs of Diabetes*, below), but there is no useful information on the absolute prevalence of these conditions among people with diabetes in Britain, largely because of ambiguity over what constitutes a diseased state. Nor is it possible to estimate the level of hypertension among people with diabetes unambiguously, because the criteria are ultimately arbitrary. On any given criteria, however, most studies have found an increased prevalence among people with diabetes. Thus Turner (1985) found that 40 per cent of male and 53 per cent of female newly presenting NIDDM patients enrolled in the UK Prospective Diabetes Study had hypertension by WHO criteria.

Nephropathy
Nephropathy mainly affects IDDM patients, probably because it is associated with diabetes of long duration. Gatling *et al* (1986) found albuminuria, the first abnormality which indicates the development of kidney disease, in 6.8 per cent of a group of diabetic patients of all ages in Britain. A proportion progress to kidney failure. Results of a national survey carried out in 1985 (British Diabetic Association, 1988) indicate that about 580 people, or about one in a thousand of the entire British diabetic population, develop end stage renal failure in a year.

Visual Impairment
Retinopathy is a major source of anxiety for diabetic patients. Estimates of its prevalence in IDDM and NIDDM populations combined range from 20 per cent to 70 per cent depending on the country, selection of subjects and the definition and means of detection of the retinal lesions. Houston (1982) has reported a survey of 714 people with diabetes in the Poole area, among whom 18.6 per cent had background retinopathy, 8.3 per cent sight-threatening retinopathy and 3.1 per cent maculopathy, while a longitudinal survey in Scotland (Foulds *et al*, 1983) estimated that 50 per cent of subjects would eventually need laser treatment for retinopathy. Diabetes is also associated with senile cataract.

Like nephropathy, retinopathy is more frequent in IDDM than NIDDM. A recent study in Italy (Segato *et al.* 1989) found that prevalence of background and proliferative retinopathy combined was 46 per cent among IDDM and 24 per cent among NIDDM patients. Because, however, the NIDDM population is realtively large, most people with retinopathy have NIDDM.

Neuropathy

Because of problems in definition, estimates of the prevalence of diabetic neuropathy vary widely, from as little as 5 per cent to as much as 80 per cent of the diabetic population, and it is not clear whether it is more commonly associated with IDDM or NIDDM or equally likely in both. Nabarro (1988) suggests that it is a clinical problem among 20 per cent of people with diabetes.

The cost of diabetes

It is well known that healthcare expenditure in any one year is concentrated on a relatively small number of people (OECD 1987). In the United States in 1982, for example, Medicare spend 54 per cent of its budget on 5 per cent of its eligible population (Riley *et al.* 1986). Similarly, in France, 5 per cent of the population covered by the Caisse Nationale de l'Assurance Maladie accounted for 63.5 per cent of its expenditure in 1980/81 (Mizrahi and Mizrahi 1985).

In the developed world, diabetes is an example of a condition affecting an identifiable group of people whose health problems and lifetime healthcare resource use are particularly high. In the United Kingdom, people with diabetes account for something over 1 per cent of the population but consume between 4 per cent and 5 per cent of healthcare resources (see Table 11 and below). Not all direct healthcare costs can be identified, but those that can be amounted to £484 million in England and Wales in 1986/7. The full cost of diabetes to the National Health Service in the United Kingdom in 1989 is probably around £1 billion.

In the United States, a recent study by Fox and Jacobs (American Diabetes Association, 1988) estimated the 'excess' direct healthcare costs of diabetes at $9,600 million in 1987, over and above 'normal' healthcare usage, Table 12. Though the authors did not compare this with healthcare spending for all causes, their figures imply that the 2.7 per cent of the United States population with diagnosed diabetes consumed about 5 per cent of the $500 billion spent on healthcare overall in the United States in 1987[5].

Most countries are moving towards a more intensively managed healthcare system. One of the keys to improved performance will be to identify groups of people with chronic diseases like diabetes which

5 The 'excess' usage is proportionately lower on these calculations in the United States than in Britain, possibly because of higher levels of ascertainment of diabetes, higher healthcare ution of the diabetic population in higher age groups where excess usage is lower.

Table 11 **Direct costs of diabetes and its complications, 1986–7 England and Wales**

	Diabetes Cost £ million	*All Causes Cost £ million*	*Diabetes as % of Total*
NHS			
In-patient (diabetes primary diagnosis)	81	6,375	1.3
In-patient (diabetes subsidiary diagnosis)	217	—	3.4
Out-patient (diabetic clinics only)	29	1,057	2.7
GP consultations (diabetes as a primary diagnosis only)	17	1,204	1.4
GP Prescriptions (diabetes as a primary diagnosis only)	35	1,960	1.8
Long-term residential and nursing care outside NHS hospitals (all residents reporting a disability from diabetes)	105	2,100	5.0
Total (where data available)	484	12,696	3.8*

*If the costs of the diabetic complications are added in for prescriptions and GP visits, and if the cost treating diabetic patients in ordinary out-patient clinics are included, it is estimated that the percentage of resources absorbed by people with diabetes would rise from 3.8 per cent to between 4 per cent and 5 per cent.

Notes **In-patient costs (diabetes primary diagnosis):** The Hospital In Patient Enquiry for 1985 indicates an average of 2,228 beds throughout the year occupied by patients with a primary diagnosis of diabetes, ICD 250 in England. Assuming no change in 1986, this is multiplied by the average cost per occupied bed in 1986/7 in acute and mainly acute non-teaching hospitals (£34,200 – Health Service Costing Returns) and further multiplied by 1.065 (the ratio of England and Wales/England hospital revenue expenditure in 1986/7) to give an estimate for England and Wales. The cost as a percentage of all non-psychiatric in-patient expenditure is lower than that found by Williams (1985) because a) diabetes bed days have declined as a percentage of the total between 1981 and 1985 and b) more activites are incorporated in the total revenue column than in the Hospital In-Patient Enquiry.

In-patient costs (diabetes subsidiary diagnosis): Williams (1985) reports that cases with diabetes as the secondary diagnosis accounted for 1.9 per cent of all admissions in East Anglia in 1981, but 4.0 per cent of all occupied beds – because of longer length of stay. This percentage is applied to the total bed occupancy of 148,633 recorded in HIPE in England in 1985 to give an estimate of 5,945 beds occupied by people with diabetes as a subsidiary diagnosis and the cost estimated as above. This may be an underestimate by more than 20 per cent, to the extent that routine hospital information systems fail to record diabetes as a subsidiary diagnosis (Williams, Fuller and Stevens, 1989). Gerard, Donaldson and Maynard (1989), using the same HIPE data, assume that length of stay for patients with diabetes as a subsidiary diagnosis is equal to the average for all admissions, implying costs about half the level shown in the Table above.

Notes continued on next page.

Out-patient diabetic clinics: Following Gerard, Donaldson and Maynard, an estimate of out-patient diabetic clinic consultations is derived from a national survey carried out by the Royal College of Physicians (1984) in association with the British Diabetic Association, which showed 3 new out-patients and 37 repeat attenders per 100,000 population per week. This implies a total of 1,032,000 out-patient attendances in England and Wales in 1986. The average cost per out-patient attendance was derived from the Health Service Costing Returns for 1985/6 for acute and mainly acute non-teaching hospitals and adjusted to 1986/7 expenditure levels, as above, to give an estimate of £27.70 per attendance.

GP consultations (diabetes): Consultations for diabetes in 1988 as a percentage of all consultations has been applied to the total cost of the General Medical Services (OHE) in England and Wales in 1986/7. The data source is the General Medical Index (GMI), published by a private market research company which monitors GP activity for the pharmaceutical industry.

Prescriptions (diabetes): Retail cost of prescriptions written following consultations for diabetes in 1988, as estimated by the General Medical Index. GMI figures for the UK have been adjusted to England and Wales pro rata with population.

Residential and Nursing Home Care: Estimated 5 per cent of residents in living in institutional settings reporting a disability attributed to diabetes (HMSO, 1988) – applied to the estimated cost of all residential and nursing care for elderly and physically disabled people outside the NHS (Laing & Buisson, 1988).

Table 12 **Direct Costs of Diabetes in the United States in 1987**

		$m
Hospital Care	Due to diabetes as primary diagnosis	1,282
	Due to chronic complications	3,267
	Due to increased intensity of care (*ie* excess admissions for non-diabetes-related causes)	484
	Additional length of stay (for these excess admissions)	1,546
	Physician visits to in-patients	352
Total Hospital Care		6,930
Nursing Home Care		942
Out-Patient Costs		1,728
Total		9,599

Source Derived from *Direct and Indirect Costs of Diabetes in the United States in 1987*. American Diabetes Association, 1988.

should receive special management attention in order to develop cost effective programmes of prevention, treatment and care.

In the Third World, the magnitude of the problem of diabetes is altogether different. The economic implications have hitherto been ignored but they represent a potentially massive burden for many developing economies (Vaughan, Gilson and Mills, 1989).

Evidence of high healthcare usage among people with diabetes

Research from a number of countries demonstrates that people with diabetes are consistently heavy lifetime users of healthcare resources.

Britain

In Britain, Williams' (1985) study of Hospital Activity Analysis (HAA) data found that the estimated 1.2 per cent of people with diabetes in East Anglia occupied 5.6 per cent of bed-days in non-psychiatric hospitals in 1981. Bed occupancy rates of the same order were found by Alexander *et al* (1988) in their analysis of South East Thames region HAA for 1985, where patients with diabetes occupied 4.7 per cent of non-psychiatric beds.

Moreover, these are underestimates to the extent that HAA fails to record co-existing diabetes as either a primary or secondary cause of admission. Thus Williams, Fuller and Stevens (1989) found in their 3 centre study of HAA that the presence of diabetes went unrecorded in 27 per cent of a sample of 751 admissions of patients known by other means to have diabetes. Under-recording has also been found in a study of SHIPS, the Scottish equivalent of HAA (Macleod *et al*, 1989).

United States

A similar pattern of high healthcare use has been observed in the United States, where a major study using 1977 data from the National Medical Expenditure Survey found that average healthcare utilisation costs among people with diabetes (for all causes – not just diabetes) were about three times higher than for the non-diabetic population (Taylor, 1987).

The American Diabetes Association's (1988) study of the costs of diabetes suggests a somewhat lower level of additional healthcare use. It calculated the risk of hospitalisation for complications of diabetes such as cardiovascular disease (the largest individual component of cost) to be 2.2 times higher among people with diabetes than in an age matched non-diabetic population. Insulin, hypoglaecaemics, syringes, tests and other special therapy pushed the out-patient cost of individuals with diabetes above the average, though data from the National Ambulatory Medical Care Survey (Harris, 1985a) indicate that physician visits, the largest single cost component of ambulatory care, are not significantly different for the diabetic and non-diabetic populations, except for the under 25 age group where first diagnosis of IDDM is concentrated. Overall, the American Diabetes Association's (1988) report suggests that the typical United States citizen with diabetes consumes about twice the amount of health care resources as an age-matched individual without diabetes.

Scandanavia

In Denmark the Frederica study covered 60-74 year olds only, 90 per cent of whom had NIDDM. They were found to use 2-3 times more hospital bed days than a control group (Damsgaard, Froland and Green 1987). Their ambulatory healthcare costs were 2.2 times as high as that of the control group. (Damsgaard, Froland and Holm 1987).

Healthcare usage in IDDM

Both the British and United States studies found extra resource usage among people with diabetes to be particularly high among younger age

groups, where people with IDDM are concentrated, and to taper off among older age groups with their heavy preponderance of NIDDM. Williams (1985), for example, found that bed usage among 0-14 year olds with diabetes was 11 times the expected level for boys and 22 times for girls. In the United States, The American Diabetes Association's (1988) report found that the relative risk of hospital admission for cardiovascular disease was 20 times as high for people under 25 with diabetes as for people of the same age without diabetes. For neuropathy, the relative risk was 90 and for ophthalmic problems, 55. However, the number of admissions of young persons for these conditions was small compared with those of older age groups, where NIDDM is concentrated. There is also a greater risk of complication of pregnancy among diabetic patients.

The 'cost of illness' framework

The framework for costing illness proposed by Rice (1966) is still broadly accepted by economists. It divides costs into three elements. Direct costs cover resources used in prevention, diagnosis, treatment and care. Indirect costs represent productive output lost by society as a consequence of sickness absence, long-term disability or premature death. Finally, there is a cost in terms of reduced quality of life borne by individuals, their families and friends. This traditional 'cost of illness' framework is adopted here, though with some important modifications.

First, the indirect costs of lost productive output are excluded from the calculations presented here. They are often calculated to be the dominant element of total illness costs, but they are of doubtful validity. In particular, it is highly questionable to use average earnings, as the cost of illness approach does, as a measure of the value of working days lost through sickness or death. In an economy with excess labour the opportunity cost of long-term non-participation in the workforce may be zero. Moreover, there are no reliable British data on absence from work caused by diabetes.

Second, and more importantly, the focus here is placed not so much on the illness, diabetes, but on the experience of *people with diabetes*. Data permitting, the analysis considers the costs of *all* illness experienced by diabetics, whether recorded under ICD code 250 (for diabetes) or not. The reason for this is that diabetes can be considered the underlying cause or a contributory cause of a whole range of conditions which are found in the diabetic population more frequently than in the general population, including hypertension, coronary artery disease, strokes, peripheral vascular disease, renal failure, retinopathy, neuropathy and ulceration of the feet. So striking is their excess use of healthcare resources, and their excess mortality (see below), that it can confidently be assumed that the great bulk of the resources spent on treating people with diabetes is ultimately attributable to diabetes and its complications.

The most recent analysis of the costs of diabetes in Britain has been published by Gerard, Donaldson and Maynard (1989) from the University of York, using 1984 data for England and Wales. More limited studies in Britain have been published by the Scottish Home and Health

Department (HMSO 1987), Alexander *et al* (1988), drawing from a study of diabetic care in an English region, and the British Diabetic Association (1988). In addition, Laing (1980) has estimated the cost of diabetes among other diet related diseases and the Office of Health Economics (OHE, 1964) attempted to quantify the costs of diabetes in the early 1960s. In Sweden, Jonsson and Persson (1981) and Persson (1986) have carried out comprehensive exercises using a similar 'cost of illness' framework to that used by Gerard, Donaldson and Maynard. Songer (1988) has written an extensive review of economic studies of diabetes, principally from the United States, quoting recent work published by the American Diabetes Association (1988) and Entmacher *et al* (1985). Bain and Ross (1987) have analysed the costs of diabetes in Canada, Triomphe *et al* (1988) in France and the Australian Diabetes Foundation (1986) in Australia.

However, only in the more recent studies in Britain and the United States have estimates been made of overall healthcare resource usage by *people with diabetes*. Economic studies carried out elsewhere are generally not comparable because they have only covered the costs of diabetes as a primary diagnosis.

Direct costs – health services

The direct costs presented in Table 11, above are mainly based on the same data sources as the York work by Gerard, Donaldson and Maynard, 1989, and for the most part simply update their 1984 figures. However, the methodology used here differs from theirs in two important respects.

First, whereas the York calculations assume that the length of stay for diabetes as a subsidiary diagnosis is the same as the average for all in-patient stays for all causes, Table 11 draws on Williams' (1985) data showing an all causes average length of stay for patients with diabetes is about double that for all patients combined. This much longer duration of stay reflects not only the nature of diabetic complications but also the fact that diabetic patients tend to stay in hospital longer for other diagnoses (Williams 1988). The same phenomenon has been documented in the United States (Sinnock, 1985; American Diabetes Association, 1988). The effect of this modification to the York calculations is to double the largest single element of direct healthcare cost.

Second, Table 11 includes an estimate of £105 million for long-term residential and nursing care outside NHS hospitals. The estimate is a fairly crude one, based on the OPCS survey of disability in Britain (HMSO 1988) where 5 per cent of residents in care homes and other institutions attributed one or more of their disabilities to diabetes. But it represents a major and growing element of the cost of diabetes.

Summing over those sectors where data are available, the aggregate cost of diabetes is estimated at £484 million in England and Wales in 1986/7. The largest single element of cost is in-patient care, estimated at £298 million, though this is probably an underestimate by 20 per cent or more because of under-reporting of diabetes in routine hospital information systems, as reported by Williams (1989) and Macleod (1989).

There are a number of omissions from Table 11 where no satisfactory

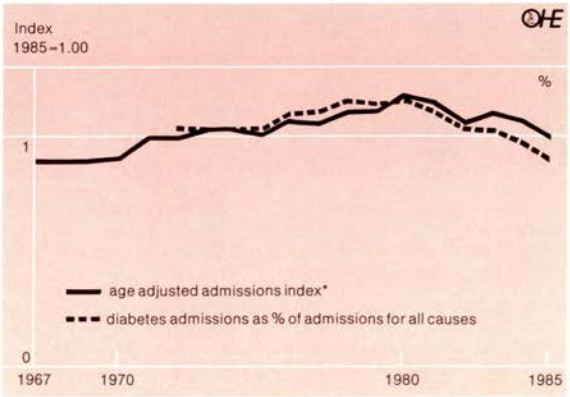
basis exists for calculating the cost of diabetes. In particular, people with diabetes are believed to make heavy demands on primary care and community services, including community nurse visits for injections and care of ulcerated feet. But there are few data on the extent of their usage. Nor is there any information on the amount of out-patient treatment that people with diabetes receive, other than in diabetic clinics. Allowing for these gaps in information, it is likely that the 1.2 per cent of British people with diabetes consume about 4 per cent to 5 per cent of all health-care resources.

Trends in costs for diabetes as a primary diagnosis – declining in-patient admissions in Britain

Robinson *et al* (1984) examined data from the Hospital In-Patient Enquiry (HIPE) in England and Wales and reported that admission rates for diabetes as the principal diagnosis had increased significantly as a proportion of all discharges between 1968 and 1978. More recent HIPE data, however, show that diabetes admissions in England and Wales reached their peak in 1980 (after adjustment for demographic change), and have been on a declining trend since then, while hospital admission rates for all causes combined have continued to grow (Figure 3). Similarly, in-patient days for the diagnosis diabetes have been declining since the late seventies, both in numbers and as a percentage of in-patient days for all causes (Figure 4).

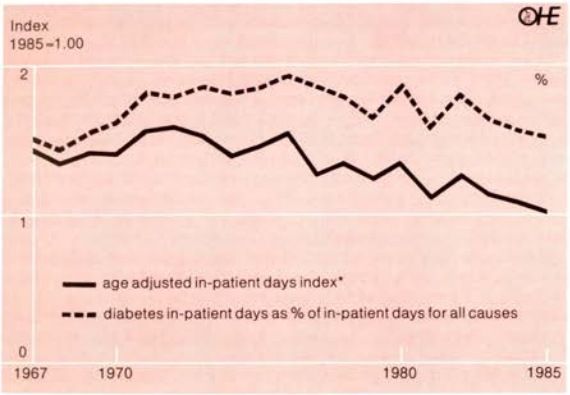
Thus in-patient costs for diabetes as the principal diagnosis are now declining in Britain, at least as a proportion of all in-patient costs.

Figure 3 **Hospital in-patient admissions with diabetes as the primary diagnosis, England and Wales**



Source HIPE.

Figure 4 **Hospital in-patient days with diabetes as the primary diagnosis, England and Wales**



*calculated by applying admissions and in-patient day rates by 5 year age groups in the base year of 1985 to the population at risk in other years.

Source Hospital In-Patient Enquiry various years.

Whether this is due to better metabolic control or a shift from in-patient to out-patient or day centre care or some other reason is not known. No such trend reversal has yet been observed in the United States, one of the few other countries where time series data are available. There, the National Hospital Discharge Surveys show that diabetes as the primary diagnosis accounted for an increasing percentage of all discharges throughout the period 1971–1983, rising from 1.45 per cent to 1.74 per cent of the total. Inclusion of diabetes as an 'other listed' diagnosis raises this share to 4.6 per cent and 7.2 per cent respectively (Sinnock, 1985).

Trends in costs for complications of diabetes

No comparable trend data are available for hospital admissions where diabetes is recorded as a subsidiary diagnosis in NHS hospitals, though it may be suspected that some complications of diabetes are generating increasing costs as criteria for acceptance into high-technology programmes are gradually relaxed to take in less fit patients. The only hard trend data on treatment of complications of diabetes relate to diabetic nephropathy. In the early 1970s this was a rarely listed cause of end stage renal failure among patients starting renal replacement therapy, but it has progressively gained in importance and has become one of the major reasons for the burgeoning number of patients on renal replace-

ment therapy in most European countries (Brunner *et al*, 1988). In 1976, 3.0 per cent of new patients on the European Dialysis and Transplantation Registry (EDTA) had end stage renal failure due to diabetes. By 1985 the proportion had risen to 10.7 per cent. Seventy-four per cent of these were diagnosed as IDDM.

Thus access to renal replacement therapy has greatly improved during the 1980s for people with diabetes. In Britain the improvement has been made possible largely through the development of Continuous Ambulatory Peritoneal Dialysis (CAPD) (Williams *et al*, 1989). A survey conducted in 1985, however, indicated that there still remained at that time a substantial reservoir of diabetic patients in Britain who were believed to be suitable for renal replacement therapy but did not receive it (British Diabetic Association, 1988a). This latent demand may add a further 70 per cent to the 1985 new diabetic patient acceptance rate onto renal programmes in the UK.

In the United States, where there is virtually unlimited publicly funded access to dialysis, diabetic patients account for a much higher proportion of demand. Eggers *et al* (1989) have reported that, out of the 28,944 Medicare funded new patients accepted in 1985 onto renal replacement therapy programmes in the United States, 8,019 (28 per cent) had diabetes.

There are no published data showing which of the complications of diabetes account for the most hospital use in Britain. In the United States, according to data presented by the American Diabetes Association (1988), cardiovascular disease accounts for over 90 per cent of those in-patient days used by people with diabetes which are attributed to specific complications of diabetes. Cardiovascular disease also accounts for about 40 per cent of in-patient days for all causes of admission among people with diabetes. Included among these admissions will be many for foot problems due to peripheral vascular disease.

Direct costs borne by individuals

Direct costs of diabetes also include those borne by the individual. In Britain, patients on insulin or oral medication are exempt from prescription charges and also receive syringes and blood and urine testing supplies free. However, diabetes may give rise to higher living expenses. In particular, the British Diabetic Association has highlighted the fact that people with diabetes need to follow a carefully controlled diet, are likely to suffer more than average from the cold – because of poor circulation and mobility – and need to take particular care of the shoes they wear because of liability to foot problems. The debate over whether or not people with diabetes face significantly increased living expenses has recently taken place in the context of changes in 1988 to Social Security entitlements, when special allowances for diet and fuel were replaced by a disability premium for people dependent of state benefits. The British Diabetic Association was unable to persuade the government to make special arrangements for people with diabetes. Knibbs (1988) explains why with respect to diet. Dietary recommendations for people with diabetes are very much in line with the COMA and NACNE recommen-

dations. Thus a healthy diet for diabetic people is the same as a healthy diet for the rest of the population. Much the same point can be made about footware. Recommendations for people with diabetes are no different from recommendations for the population as a whole, though those with diabetes are more vulnerable to problems if they fail to meet them.

Of the two dietary costing exercises quoted by Knibbs, one (Hanes and De Looy, 1987), found that the cost of a diabetic diet for an adult was not significantly different from that shown by the National Food Survey for lower income adult only households. Hall (1987), did find that younger diabetics are faced with significantly increased food costs, up to about 50 per cent higher than the rest of the population, but that pensioners are not. Knibbs concludes that although a strong case can be made for increased food allowances for children and young people, the case for extra allowances for pensioners is more difficult to argue.

Though people with diabetes may not have to spend more money than average because of their condition, they may have to spend substantial amounts of time in managing it and preventing its complications. Triomphe has proposed a novel technique of 'time budgeting' in order to identify the magnitude of this element of personal cost faced by people with diabetes, but no data have yet been published.

Employment

Robinson (1989) has reviewed the situation throughout Europe and found that people with diabetes face a much greater range of employment restrictions and problems than others. Generally, people receiving medication for diabetes, whether oral or insulin, are not allowed to join the armed forces, the police, the fire brigade or merchant navy, fly aeroplanes or drive main line passenger trains. People whose diabetes is well controlled by tablets and/or diet are usually able to continue driving heavy goods or public service vehicles for a living. But people dependent on insulin are usually not. They may also be barred either by regulation or custom and practice from other jobs where unpredictable attacks could put themselves or other people at risk.

A recent survey of a sample of IDDM and NIDDM clinic attenders from 8 towns in Britain (Robinson *et al*, 1989a, 1989b) found that unemployment rates for men with diabetes were, at 22 per cent, significantly higher than for non-diabetic controls, at 8 per cent. Similarly, in the United States, the 1978 Survey of Work and Disability has shown that 33.7 per cent of the diabetic population of working age was severely disabled and unable to work regularly or at all, compared with 8.8 per cent for the general population (Drury, 1985).

Robinson points out that in a time of continuing unemployment, where training for many jobs is expensive, it is unrealistic to expect an employer not to discriminate against groups known to be employment risks. A particular problem for employers may be extended periods of sickness absence among a minority of employees with diabetes. According to a British Diabetic Association survey (Robinson, 1989b) the proportion of people with diabetes reporting time off was no higher than for

controls, but 29 per cent of diabetics compared with 16 per cent of controls had taken 20 days or more off sick in the last year and this difference was highly significant.

Welfare effects – death and disability

Evidence on reduced life expectancy – IDDM

Reduced life expectancy among people with diabetes, with the associated welfare costs to the individuals themselves, their families and friends, is well documented, though there remains uncertainty over the number of years by which life expectancy is reduced.

IDDM is associated with a particularly high loss of life expectancy. Thus Donovan *et al* (1984) reported the experience of just under 2000 patients, diagnosed as children between 1950 and 1981, who showed a seven-fold excess mortality compared with the general US population. Mortality experience was worse in males than females and worse in blacks than in whites. A surprisingly large proportion of deaths in this IDDM population (just under 20 per cent) were the result of acute complications (such as ketoacidosis), this being the most important single cause of death under the age of 20. But for all age groups combined, renal disease was the largest single cause (45 per cent of all deaths). Data from the European Dialysis and Transplant Association confirm the high risk of renal failure among people with IDDM. Two thirds of diabetic patients on renal replacement therapy are diagnosed as IDDM, despite accounting for only about one fifth of the diabetic population. Their 5 year survival on treatment is relatively poor, ranging from 51 per cent for 15-34 year olds (compared with 82 per cent for non-diabetics) to 13 per cent for diabetics over 65 (compared with 34 per cent for non-diabetics), Brunner *et al* (1988). Coronary heart disease is also a major contributor to mortality in IDDM. Veikko and Tuomilehto (1989) estimate excess mortality to be between 2 and 8.5 fold compared with the non-diabetic population, though calculations are vitiated by the difficulty of distinguishing between IDDM and NIDDM populations at risk.

Life expectancy tables for people with diabetes have been constructed in the United States, but they vary widely in their estimates of lost life years. Thus a study of excess mortality among life insurance applicants over the period 1950–71 found that people who developed diabetes before the age of 15 (*ie* an IDDM population) lost 27 years of life compared with the general population (Table 13). In contrast, life expectancy derived from death certificates in Iowa and Pennsylvania, where good estimates of diabetes prevalence are available, indicate a loss of less than 10 years of life expectancy for those whose diabetes was diagnosed young (Bale and Entmacher, 1977).

Evidence on reduced life expectancy – NIDDM

Panzram (1987) has reviewed the evidence of NIDDM. This is summarised in Table 14 which indicates excess mortality across all age

Table 13 **Excess mortality rate among diabetic insurance applicants versus general population, 1951–70, and expectation of life.**

Age (Years) at Onset of Diabetes	*Ratio, Diabetic Mortality Rate Versus General Population Rate**	*Expectation of Life (Years)*	
		Diabetics	*General Population*
Under 15	11.27	32	59
15–19	9.26	33	56
20–29	4.43	33	49
30–39	3.44	28	39
40–49	3.01	20	30
50–59	2.13	17	23
60–70	2.34	11	16

*Expected deaths in general population based on Equitable's mortality tables 1958–1963.

Source Goodkin, G. Mortality factors in diabetes. J Occup Med 17: 716–21, 1975.

groups of about 50–100 per cent. He emphasises, however, the need for caution in interpreting the data, particularly in view of changing criteria for diagnosing NIDDM. Most of the longitudinal and cross-sectional studies on diabetic populations initiated in the sixties and seventies, he points out, included large numbers of patients whose condition would today be labelled as 'Impaired Glucose Tolerance' rather than NIDDM on WHO criteria.

Coronary heart disease is the most frequent cause of death in NIDDM and the age adjusted cause-specific mortality rate is 2 or 4 times higher than in comparable non-diabetic control subjects, Table 15. The second most important cause of death is cerebrovascular disease, because of its close relationship to frequently co-existing hypertension. A WHO committee (WHO 1985) has estimated that stroke accounts for 15 per cent of deaths among NIDDM patients. Panzram (1987) points out in his review that there are few prospective and representative studies of the incidence and prevalence of stroke in diabetic patients (Jarrett (1985), Pyorala (1987)), but that the data that have been published indicate there is about a 2- to 4-fold greater risk of death from cerebrovascular disease in both sexes, than in non-diabetic individuals. In contrast with IDDM, renal disease is a minor cause of death in NIDDM patients. In studies reviewed by Panzram (1987) it did not account for more than 5 per cent of deaths in caucasian NIDDM populations.

All studies agree that the degree of excess mortality among people with diabetes declines with increasing age (Tables 14 and 16). Panzram (1987) reports that a 10 year cohort study within the defined diabetic population of the Erfurt district did not find any significant differences in the death rates of NIDDM patients beyond the age of 75 as compared with non-diabetic control subjects.

Table 14 **All-cause excess mortality in study populations consisting predominantly or exclusively of Type 2 (non-insulin-dependent) diabetic patients**

Author	*Year*	*Region*	*Age at diagnosis*	*Excess mortality*		
				Males	*Females*	*Total*
Goodkin	1975	USA	40–49	—	—	3.01
			50–59	—	—	2.13
			60+	—	—	2.34
Krolewski *et al*	1977	Warsaw	30–49	2.13	1.61	
			50–68	1.17	1.22	
Shenfield *et al*	1978	Edinburgh	40+	1.15	1.41[a]	
				1.53	1.90[b]	
Panzram and Zabel-Langhennig	1981	Erfurt	40–49	1.80	1.86	
			50–59	1.47	1.81	
			60–69	1.40	1.37	
			70–79	1.09	1.15	
Reunanen	1983	Finland	Type 2	2.0	2.7	
Sasaki *et al*	1983	Japan	Type 2	1.50	1.39	
Fuller *et al*	1983	British Diabetes	45–64	1.98	2.72	
		Assn Cohort	65+	1.38	1.97	
Barrett-Connor and Wingard	1983	California	40–79	1.5	2.3	
Zwaag *et al*	1983	Atlanta	45–54[c]			2.07
		Memphis	55–64			1.57
			65–74			1.26
			75+			1.07
Jarrett	1985	Whitehall	Type 2	2.38		

[a] Treatment with diet only; [b] treatment with oral drugs; [c] age at cohort-entry.

Source G Panzram. Mortality and survival in Type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia (1987) 30: 123–131.

Table 15 **Prospective population-based studies on coronary heart disease mortality risk in predominantly middle-aged diabetic patients**

Study location	*Year*	*Age (years)*	*Follow-up (years)*	*Mortality risk ratio*[a] *Males*	*Females*
Du Pont Company	1970	<20–64[c]	10	2.87[b, d]	
Israel	1977	>40	5	3.4[b, d]	
Framingham	1979	45–74	20	1.7	3.3[c]
Evans County	1980		4.5	1.0	2.8[b]
Rancho Bernardo	1983	40–79	7	2.4	3.5[c]
Warsaw	1984	18–68	9.5	1.33	1.65[b]
Whitehall	1985	40–64	10	2.45	[c]
Chicago	1986	35–64	9	3.8	4.7[c]
Finland	1986	40–69	11	2.0	4.1[b, d]

[a]Rancho Bernardo and Warsaw identified ischaemic heart disease; Israel identified myocardial infarction; all others identified coronary heart disease: [b]relative risk (observed/expected death proportion, standardized mortality ratio) Evans County and DuPont Company not age-adjusted; all others age-adjusted: [c]multiply-adjusted risk including age and major coronary heart disease risk factors with inter-study variations in covariates and statistical methods: [d]newly diagnosed diabetic patients: [e]among a total of 370 diabetic patients, only 9 patients aged below 40 years.

Source G Panzram. Mortality and survival in Type 2 (non-insulin-dependent) diabetes mellitus. Diabetologica (1987) 30: 123–131.

Table 16 **Age-related reduction of life expectancy (mean of years lost in diabetic patients**

Age (years)	*Marks and Krall 1971*	*Goodkin 1975*	*Panzram and Zabel-Langhennig 1981*
10/<15	(17)	27	—
15–19	16–17	23	—
20–29	12–14	16	—
30–39	10–11	11	—
40–49	8–9	10	7–8
50–59	6–7	6	5–6
60–69	4–5	5	3–4
70+	—	—	3

Source G Panzram. Mortality and survival in Type 2 (non-insulin-dependent) diabetes mellitus. Diabetologica (1987) 30: 123–131.

Trends in mortality: the effects of coding for death certificates

It is not clear whether, and to what extent, excess mortality among people with diabetes is declining. In the United States, mortality rates for diabetes dropped from 18.9 to 14.9 per 100,000 between 1970 and 1983. But these figures include only deaths where diabetes is recorded as the principal underlying cause, and take no account of the majority of deaths among people with diabetes which are due to cardiovascular, renal and other diseases.

In Britain, recent time trends are confounded still further by recording changes. Thus Robinson *et al* (1984) reported a significant decline in mortality for diabetes as the underlying cause among females in England and Wales from 1968–1980, though not among males. Since then, however, there has been a sudden surge in recorded diabetes mortality, Figure 5. In fact, the phenomenon is almost certainly an artefact of the recording system and an illustration of the pitfalls of time series analysis. In 1984 the Office of Population, Censuses and Surveys (OPCS) applied a change in coding rules such that for certain conditions recorded as the 'underlying' cause of death in Part I of the death certificate – pneumonia for example – the secondary cause mentioned in Part II of the death certificate should be coded as the underlying cause for the purposes of mortality statistics. A further change was implemented in 1985 which would have had the effect of transferring more Part II mentions of diabetes to underlying cause for publication in the OPCS statistics. Following the coding changes, the Standardised Mortality Ratio for diabetes in England and Wales rose by over a half between 1983 and 1986. The increase affected only age groups over 55 was by far the greatest in the very old age groups, where conditions like pneumonia are most likely to appear on Part I of death certificates.

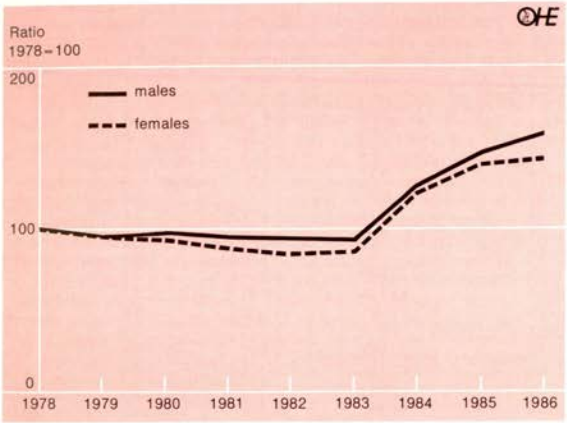
Numbers of Deaths and Life Years Lost

Just as it has been assumed that the bulk of direct costs of treating diabetics is ultimately attributable to diabetes – whatever the principal recorded diagnosis, so it is assumed that the great majority of deaths where diabetes is mentioned, whether in Part I or Part II of the death certificate, are ultimately attributable to diabetes. Table 17, therefore, includes not only the 7,912 deaths (1.4 per cent of all causes) where diabetes is recorded as the underlying cause but also the deaths where diabetes is mentioned in Part II of the death certificate, to bring the overall total to 22,919 (3.9 per cent of all causes) in England and Wales in 1986. About two thirds of these additional diabetes associated deaths are recorded as due to circulatory disorders, including heart attacks, stroke and peripheral vascular disease (British Diabetic Association 1988).

Table 17 also shows the number of future life years lost in 1986. This amounted to 88,000 person years in 1986 (1.2 per cent of all causes) for diabetes as the underlying cause only and 261,000 person years (3.5 per cent of all causes) for diabetes mentioned at all on the death certificate.

According to data from two cohorts whose mortality was followed during the sixties and seventies (Shenfield *et al*, 1979; Fuller *et al*, 1983), only 67 per cent of death certificates of people with diabetes mention

Figure 5 **Standardised mortality ratio for diabetes, England and Wales, 1978–86**



Source Office of Population Censuses and Surveys
Note The increase from 1983 is due to coding changes – see text.

diabetes at all. Adjusting for this distortion would increase the number of deaths among people with diabetes from 23,000 to 34,000 (5.9 per cent of all deaths) in England and Wales. In effect, this simply amounts to saying that 5.9 per cent of people have clinically diagnosed diabetes by the end of their lives, a figure which fits reasonably well with age-specific prevalence data.

An unexpected feature of Table 17 is that diabetes is less important as a cause of life years lost than as a cause of death. Since diabetes is known to lead to a reduced expectation of life, the reverse should be true. The only way of explaining this apparent inconsistency is to assume that deaths occurring among diabetic people where diabetes is not mentioned at all are concentrated among the younger age groups. One possible group of causes in which this may be occurring are injuries and poisonings which make a substantial contribution to early adult mortality in the general population but which, if unconnected with diabetes in a young diabetic person, would be registered without mention of diabetes.

Disability

Long-term disability is the other major element of personal cost. Data on disability by disease in Britain, however, is very limited. The recently

Table 17 **Premature death and future life years lost from diabetes, England & Wales 1986**

	Future life years lost to age 90		*Deaths*	
Age	*Underlaying cause*	*Mentioned* cause*	*Underlying cause*	*Mentioned* cause*
<1	148	148	2	2
1–4	71	71	1	1
5–9	73	146	1	2
10–14	337	337	5	5
15–19	657	1,026	11	17
20–24	803	1,085	14	19
25–29	809	1,270	16	25
30–34	1,045	1,711	23	38
35–39	1,176	2,627	29	65
40–44	1,326	3,050	48	105
45–49	2,371	6,604	76	212
50–54	3,853	11,637	143	435
55–59	6,091	20,105	272	904
60–64	10,215	34,243	479	1,636
65–69	11,783	38,723	770	2,553
70–74	15,204	48,601	1,256	4,021
75–79	15,466	46,080	1,644	4,915
80–84	11,682	31,560	1,618	4,381
85–89	4,939	12,368	1,005	2,517
90–94	0	0	416	907
95+	0	0	83	159
All ages	88,049	261,391	7,912	22,919
Diabetes as % all deaths/ years lost	1.18	3.50	1.36	3.94

*Mentioned causes include underlying causes.

Source Derived from *Mortality Statistics: cause*, OPCS Series DH2.

published OPCS study of disability, HMSO (1988a), found that 2 per cent of people living in private households and 5 per cent of people living in institutions have some degree of disability which they attribute to diabetes. This implies about 1,100,000 people disabled with diabetes living in the community and a further 25,000 people disabled with diabetes and living in a residential or nursing home or long-stay hospital ward. The OPCS results, however, are at odds with other epidemiological work, see above, which puts the overall number of people with clinically diagnosed diabetes in Britain at a maximum of 750,000, plus the unknown number who may be developing complications and may be

seen by their doctors for these rather than the classical diabetic symptoms.

No data have been published by OPCS on the distribution of disability by severity category. Nor are there any data on the incidence or prevalence of disability arising from heart attacks, stroke, peripheral vascular disease, retinopathy, nephropathy or any other complication arising from diabetes.

Somewhat better information on disability is available in the United States, where the results of the 1977 National Health Interview Survey found that 41.3 per cent of people with diabetes reported limitation on activity compared with 18.6 per cent for the population as a whole.

But no country appears to maintain the sort of statistical series which would indicate whether, and to what extent, improved management of diabetes is reducing the burden of disability. It might be expected, for example, that the development of laser treatment for retinopathy would have reduced new registrations for blindness or partial sight in the mid and late eighties. But such information as is available in Britain is either out of date or not recorded in a way that would allow comparison of trends over time (HMSO 1988b). The same can be said of most of the other major complications of diabetes, where a veil of statistical ignorance precludes any assessment of the contribution of healthcare to the welfare of people with diabetes.

Organisation and delivery of care

Diabetic people have high levels of morbidity and they are high users of healthcare services. Their patterns of illness are to a large extent predictable and a planned approach to management of health problems should be well suited to this population, in the search for opportunities for more effective resource use and for improving length and quality of life.

Effectiveness of intervention

Primary prevention

Primary prevention of IDDM is a theoretical possibility with the use of immunosuppressive agents to prevent the body's immune response to viral infections damaging the beta cells in the pancreas. But the balance of risk is at present weighted against this approach. Primary prevention of NIDDM would be assisted by diet and weight control, but understanding of its aetiology is as yet inadequate to indicate a clear preventive strategy. Pancreatic transplantation might conceivably offer a 'cure' for diabetes in the way that insulin and other therapies do not. But safe and reliable transplantation remains a distant prospect.

Secondary prevention

The effectiveness of secondary prevention in both IDDM and NIDDM is not in doubt, though such research as has been conducted has typically not incorporated an economic component and the costs and benefits

have not been assessed in terms of quality adjusted life years (QALYs) expected per unit cost. It is believed, though not proven, that maintaining near physiological blood glucose levels is the key not only to avoiding acute crises but also to preventing the development of long-term complications of both IDDM and NIDDM (Pirart, 1978). Thus behavioural change through education allied with appropriate medication are the cornerstones of healthcare for people with diabetes (Connor, 1984). In the event of the strategy of primary or secondary prevention failing, there is strong evidence that early medical or nursing treatment of many established complications can reduce morbidity and costs.

In retinopathy, the detection of early disease followed by laser treatment prevents blindness (Köhner and Barry, 1984). It has also been estimated that intensive management of diabetic foot problems can reduce the amputation rate by 50 per cent (Edmonds *et al*, 1986) and anticipatory care generally for peripheral vascular disease can reduce morbidity and costs.

Screening for small quantities of protein in the urine, which is one of the early signs of renal damage, followed by advice on diet and/or a change in medication, may be useful in delaying the development of nephropathy. There is some evidence that improved glycaemic control by the use of continuous subcutaneous insulin infusion (CSII) may reduce the incidence, or at least delay the onset, of this serious complication which is a major contributor to treatment costs and mortality in IDDM. Also, Bjorck *et al* (1986) have reported arresting the deterioration of glomerular function among 14 hypertensive IDDM patients given ACE inhibitors. If these results can be repeated in the long-term it will represent a major advance in treatment of people with IDDM.

Screening for and treatment of moderate to severe high blood pressure is to be advocated in the diabetic population because of their high frequency of hypertension and high risk of preventible cerebrovascular and coronary heart disease. As regards mild hypertension, the UK Medical Research Council trial, MRC (1985), found that large numbers of mildly hypertensive patients have to be treated over long periods to derive any benefit. But the trial did not recruit people with diabetes and the MRC results cannot necessarily be extrapolated to them. Further trials are urgently needed in the diabetic population (Ritchie and Atkinson, 1986).

Some commentators have argued more generally that the amount of resources spent on diabetes research is inadequate in relation to the burden the disease imposes on society. It has been estimated, for example, that in 1985 only £3.3 million was spent on diabetes research in the UK compared with £130 million in the United States (British Diabetic Association, 1987).

Access to healthcare services

Information is very patchy on the extent to which diabetic patients in Britain have access to the various components of prevention, education, management and treatment of complications, whether on a planned

basis or otherwise. The proportion attending hospital clinics for diabetes care is low – about 50 per cent for city practices and 20-30 per cent in urban and rural areas (Williams 1986). But little is known of the proportion attending *any* clinic, whether in hospital or in general practice.

Access probably varies widely, depending, for example, on whether the patient's GP has an interest in diabetes. There are indications that, in practices which do not have a particular interest in the management of diabetes, around 50 per cent of clinically diagnosed patients have no future appointment arranged to see anyone about their diabetes, whether a hospital physician, general practitioner, private physician, diabetes specialist nurse or dietician. (Williams *et al*, unpublished).

Alexander (1988) has described the level of services in the South East Thames region of England. He found that all districts had access to laser treatment and to laboratory services, though retinopathy screening was unavailable in 10 out of the 15 districts and 5 had no formal education programme. Particular emphasis was laid on inadequate staffing levels. Consultant sessions in diabetes were 40 per cent of the level recommended by the British Diabetic Association and the Royal College of Physicians and specialist nurse staffing was 30 per cent of the recommended level.

In the particular case of renal failure, a national study has estimated that only 60 per cent of diabetic patients who could benefit from renal replacement therapy get it (British Diabetic Association 1988a). However, there must be some doubt over the appropriateness of extending access to treatment to include people with ever more advanced multisystem disease associated with diabetes. Survival rates among these patients, and the degree of rehabilitation, can be poor compared with non-diabetic peers and this presents those working in diabetic and renal clinics with a major dilemma in deciding how resources should be allocated.

Delivery of Healthcare

As with many other areas of healthcare, there appears to be a good case for more resources to be devoted to diabetes. But, probably of more relevance, there may be substantial benefits to be derived from using existing resources in different ways. Persson (1986) in his study of the costs of diabetes, points out the major difference in resource use between Sweden, where the ratio of institutional to non-institutional costs is 1.7:1, and the United States where the ratio is reversed. He then poses the question – could increased use of resources in non-institutional care result in better control of diabetes and perhaps lower treatment costs overall? The answer must, in the present state of knowledge, be 'not proven'. In principle, most acute episodes of hospital treatment are avoidable by better control of blood sugar levels and many complications are preventible by anticipatory care, both of which depend primarily on education and community services. But little rigorous research has been conducted.

The best review of the effectiveness of education programmes has been carried out in the United States by Kaplan and Davis (1986) and does not lend much support to their value, in the United States at least. In the light of the proposal by the American Diabetes Association that out-patient diabetes education and nutrition counselling should be eligible for third-party payment, the authors critically reviewed 13 studies. They found that only two had control groups and neither of these was randomised. Only 4 studies showed programme costs and in some cases total spending had actually increased. It should be emphasised that the results of their review demonstrate the lack of good research in this area and not that patient education is proven to be ineffective. Many clinicians can recall examples where good advice to patients (such as avoiding tight shoes) could have prevented complications if the advice had been followed.

Diabetes Centres and Community Care

In Britain, much of the debate over the merits of increased emphasis on education and community services has taken place in the context of Diabetes Centres. These have been set up in a number of districts to replace hospital out-patient clinics with a more convenient, accessible, community based service (Day and Spathis, 1988; Day *et al.* 1988; Boucher *et al.* 1987; Brown, 1987). Assessment of these centres is at too early a stage to allow conclusions to be drawn on cost effectiveness (Day *et al.* 1988), though clearly they are an interesting innovation. Community services for diabetes have also been developed within the framework of general practice, in mini-clinics, with the hospital diabetes team in some cases making regular visits to general practice surgeries and conducting clinics jointly with their general practice colleagues. Most of these innovations preceded the move towards diabetes centres. The earliest documented schemes in the United Kingdom were those in Birmingham (Malins *et al.* 1971), Wolverhampton (Thorn, 1971) and Poole (Hill, 1976). These papers described, respectively, regular visits of the hospital team to participate in joint clinics in general practice, general practice 'mini-clinics' (regular sessions set aside for diabetes care by the general practice team) and 'community care' (a large number of practices in one geographical area each devoting a number of appointments specifically to the organised care of their patients with diabetes). Since then a number of studies have been published comparing hospital and general practice care for diabetes (see, for example, Hayes and Harries, 1984). These studies illustrate the superiority of hospital clinics over *standard* general practice care. But when general practitioners specifically organise diabetes care, there is nothing to choose between them and hospital clinics in process and outcome (Williams, 1986). Thus the proponents of mini-clinics maintain that diabetes care is properly based in general practice and that interested GPs with specialist nursing assistance and some additional equipment can offer most if not all of the services provided by diabetes centres. However, only a minority of GPs have the interest or the experience to operate mini-clinics in most health districts. Finally, some commentators have advocated improvement of

hospital out-patient clinics, where all services can be provided on site most economically.

The Future

The White Paper on the NHS, *Working for Patients* (HMSO, 1989a), has proposed a number of reforms which will have the effect of encouraging, even forcing, more flexible development of healthcare services and giving greater scope for a mix of styles of care. Whether this will act on balance to the benefit or detriment of people with chronic health problems like diabetes is not yet clear. Much depends on how the details of government policy are modified in the light of discussion and experience over the next few years and under what incentives healthcare providers find themselves operating.

Self-Governing Hospitals

The White Paper is principally concerned with developing a framework under which an internal market for elective surgery can develop. Self-governing hospitals are expected to play a key role here. This has provided a focus for criticism that they will shift their resources to revenue earning surgery to the detriment of groups of patients such as people with diabetes whose main requirement is for community health services and medical out-patient and in-patient treatment. Such a shift in priorities may be a risk, particularly for London teaching hospitals with a wide private and international market to tap. Most hospitals, however, whether self-governing or not, will continue to depend almost entirely on money spent by health authorities. The pattern of resource allocation that develops in the future will thus depend primarily on how health authorities discharge their role as arms length purchasers of services. Under an internal market system hospitals will do what health authorities pay them to do. It is quite possible, for example, that health authorities will pay self-governing hospitals in highly populated areas to offer packages of hospital and community support for diabetes and other chronic conditions, extending outside their immediate catchment zones.

General Practice

The future of diabetes care in general practice is particularly intriguing. There appears to be a sound case (see above) for encouraging general practitioners to develop a special interest in organised diabetes care and to make this specialisation widely known to local patients. The evidence suggests that not only would diabetic patients choosing such a GP receive a better quality of care but demands on hospital services could be reduced.

The recent addition of an extra sessional payment for GPs, in the 1989 revision of contracts, may encourage some GPs to foster a special interest in organised general practice care for diabetes, though a pessimistic view is that such a sessional payment would encourage some GPs to establish practice based diabetic clinics in name only. Clearly it is important to ensure that qualification for any payment depends on meeting

appropriate professional standards and that the full effects are monitored by Family Practitioner Committees (FPCs). The risk of abuse should not in itself be seen as a barrier to special or incentive payments to encourage particular aspects of care, which are a well established part of general practice.

Under the White Paper proposals, general practices of a certain size will be able to opt for Practice Budgets. This will give them the freedom and incentive to exploit trade-offs between in-practice and hospital outpatient care. Practice budgets could thus open up a range of possibilities for extending the experiments of the 1970s and 1980s in providing programmes of diabetes care in mini-clinics and diabetes centres, and budget holding general practices might become a major focus of innovation in diabetes care. It is worrying, however, that the detailed proposals for practice budgets as set out in Working Paper 3 (HMSO 1989b) may strongly discourage GPs seeking to enrol diabetic and other chronically sick patients. The Working Paper suggests that the amount of the practice budget should be set at a point between the cost of services provided by the practice in the previous year and the average for the district as a whole. This would make allowance for historically high costs. But there is no provision for money to 'travel with the patient' by making the practice budget reflect the marginal cost of any *new* chronically ill people added to the list. Faced with this disincentive it is hard to envisage budget holding GPs with a special interest in diabetes seeking to attract diabetic patients with offers of organised care. If this is the case, an important opportunity for extending choice to chronically ill people will have been missed.

For the bulk of general practices not operating practice budgets, the proposal for indicative prescribing budgets, as set out in Working Paper 4 (HMSO 1989c), also seems likely to discourage GPs from actively seeking new patients with diabetes or other chronic illnesses. It is stated in the Working Paper that budget setting FPCs will take account of 'special interests' of practices, and this could cover diabetes and other chronic illnesses. But it seems unsatisfactory to rely on FPCs to redress problems arising from fundamentally inappropriate incentives. If choice is to be enhanced for chronically ill people, what seems to be required is a clear mechanism for recognising the cost of their care and adjusting budgets accordingly. A modification along these lines would in no way run contrary to the main thrust of the White Paper proposals.

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